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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

MAY 1944

CANCER OF THE COLON

HENRY CAVE

Attending Surgeon, The Roosevelt Hospital

CANCER of the colon is amenable to surgical extirpation. Only in so far as diagnosis is concerned is it a medical disease. It has been and can be diagnosed by the physician, but it should not be treated by him. All physicians should be keenly aware of the early signs and symptoms if any exist. All new chemotherapeutic measures have failed to retard in any measure or influence its development. Irradiation with x-rays or radium on a primary colonic growth is valueless. If attacked surgically before metastasis has taken place, a longer period of cure can be expected than in cancer of any other part of the gastrointestinal tract. It is considered usually, a disease of advancing years; but not infrequently it is discovered in the third and even the second decades of life. When found in the younger age groups it is usually of a violently malignant nature and the morbidity and the mortality are high. Deaths from cancer of the colon are second to cancer of the stomach in malignancies of the gastrointestinal tract.

In the City of New York with a population of 7,300,000 persons in the year of 1942, the Bureau of Vital Records and Statistics shows that

* Read before the 16th Graduate Fortnight of The New York Academy of Medicine, October 21, 1943.

1,962 individuals died of cancer of the stomach. In that same year 1,616 people died of cancer of the colon and also in this same year there were 911 people who died of cancer of the rectum.

I have been unable to find any statistical data which would suggest that cancer of the large intestine is on the increase. Yet due to the ever increasingly laudable attitude of the laity, towards the value of the x-ray as a precise aid in diagnosis, many more colonic tumors are discovered suggesting perhaps an increased incidence.

This Graduate Fortnight fostered by The New York Academy of Medicine is attended largely by physicians with a scattering of surgeons, therefore, this presentation will deal mainly with the physiology, the symptomatology and the methods of early diagnosis and not operative procedures except in generalities.

Anatomy and Physiology

In order to appreciate adequately the symptom-producing mechanism of colonic growths it seems timely to re-emphasize briefly certain anatomic and physiologic facts.

This discussion does not include the rectum. The colon begins in the right iliac fossa and ends opposite the body of the third sacral vertebra, where it fuses with the rectum. The size of the colon and the thickness of its musculature has considerable bearing on the rapidity with which symptoms appear. The cecum is large, thin-walled and its diameter is approximately 6 cm. as contrasted with the diameter of the sigmoid which is 2.5 cm. The thickness of the wall increases from the cecum down to the descending colon and the sigmoid. Fecal matter which is poured into the cecum through the ileo-cecal valve is quite liquid and as it nears the sigmoid segment it becomes thicker. Due to the anatomic arrangement of the ileo-cecal valve, malignant involvement of the cecum in this region causes obstruction early. Tumors particularly the fungoid type growing in the cecal wall have plenty of room for development and expansion, hence obstruction comes late, if ever. Fungoid, ulcerating and cicatrizing growths of the left colon and sigmoid all necessarily produce obstruction earlier due to the smaller caliber of this segment of the large bowel.

Symptoms

In discussing symptoms, it might be well to divide the colon into

two halves: (1) the cecum, the ascending and right half of the transverse colon; (2) the left half of the transverse, the descending and the sigmoid colon. It is a noteworthy fact that cancer of the colon, in its earlier stages usually produces symptoms which are decidedly vague, frequently bizarre and often insidious. I question whether or not authors writing on the early diagnosis of cancer of the colon are right in assuming that malignancy of the colon is ever diagnosed early. It is the complications of cancer and not the growths themselves which give symptoms.

There are various other lesions of the colon and diseases of the viscera outside the colon which produce symptoms similar to those of neoplasms of the large bowel, namely – diverticulitis, tuberculosis, ulcerative colitis, also chronic disease of the appendix, chronic cholecystitis, peptic ulcer and intermittent mild attacks of subacute pancreatitis.

When the lesion is once present, and all too frequently in a palpable form, cancer of the right colon presents symptoms of so-called "dyspepsia," marked anemia with loss of weight and strength. The earliest period of manifestation of cancer of the cecum and of the ascending colon may be a vague sense of bloating. Sometimes a mucous diarrhea will occur and the patient is aware of an alteration, even though slight, of the bowel habits. The old text-book story of alternating constipation and diarrhea frequently means that the growth has become of considerable size, far advanced, and certainly could not be classed as an early symptom, but as a later manifestation of the disease. The anemia, usually severe is by far the most characteristic feature of right sided growths. Any patient suffering from marked anemia, even though there have been no symptoms or signs of malignancy of the colon, should be investigated for this disease. Why is it that the anemia is more marked with cancer of the cecum and ascending colon than it is with cancer of the left half of the colon? We all know that it is seldom that sudden sharp hemorrhage springs from a right sided growth; hence, this severe anemia must be due to the fact that the growths are usually large in the right colon, the oozing surface extensive and that there is an increased absorptive area for toxic substances. Tenderness and the presence of a palpable mass in the cecum or the ascending colon is generally a late sign, yet there have been a few instances where we have elicited a history of pain and local tenderness in the early growths of this segment of the large bowel.

In cancer of the left half of the colon, the efforts to force the more solid fecal material down into the rectum past the partially or completely obstructing lesion which narrows the lumen of the descending colon produces pain. Increasing constipation is an almost constant complaint. The patients complain of bloating, abdominal distention and a feeling of general discomfort. I have observed a few instances of a vague intermittent slight distention as the only symptom of an early malignancy of the lower sigmoidal segment, and so often the discomfort is relieved by the passage of flatus.

Obstruction, either acute or of a chronic nature, may be the earliest symptom denoting the presence of a tumor of the left colon. We have been impressed by six instances of obstructive lesions of the left colon where the only symptom was pain and a feeling of localized distention in the right lower quadrant. All of these patients were operated upon primarily for appendicitis, and later came to secondary operations for the growth in the left half of the bowel. The reason for this pain in the lower quadrant, is due to the thinness of the cecal wall, the back pressure from the partial obstruction distends the proximal bowel especially the cecal head; the distention being the pain-producing mechanism.

Annular carcinoma of the sigmoid segment is capable of producing pain in the right upper quadrant. In one patient the pain was so severe she was operated upon for gall bladder disease. The gall bladder was found to be normal and a tight band across the pyloric end of the stomach was divided. Relief from vomiting was assured this patient; but, after three weeks time when the patient had returned home, right upper quadrant pain and persistent vomiting necessitated further study. Repeated and carefully taken roentgenograms failed to reveal the presence of a small tumor in the sigmoid which was found when this patient was subjected to an exploratory operation without a preoperative diagnosis having been made.

In order to obtain information which might prove helpful in the early diagnosis of neoplasm of the colon, Scudder Winslow of our Interne Staff has carefully reviewed and analyzed eighty-four of our case histories from the First Surgical Division of The Roosevelt Hospital. The cases were treated during the past decade (October 1, 1933 to October 1, 1943). The majority of these patients were individuals whom we see in the wards of our metropolitan hospitals, many in the

older age group, in poor physical condition, some undernourished and old for their years. Our findings were disappointing; for many were in the advanced stages of the disease when admitted.

Fifty per cent were either acutely or chronically obstructed upon admission. Forty-three or one-half of the total number complained of change in bowel habits, forty-three complained of abdominal discomfort of greater or lesser degree, nine localized their pain in the right lower quadrant. The average age of this group of patients studied was sixty years. There were an equal number of males and females. Loss of weight was frequently noted, usually ranging between ten to thirty pounds. The disease for the most part was self evident in the larger proportion of cases, not only from their general appearance, their cachexia but the presence of a tumor mass and signs of obstruction and positive findings by x-ray. Seventy per cent had well marked evidence of neoplastic disease as evidenced either by obstruction or by the presence of a palpable mass. Certainly there were but few instances where it could be stated that these patients sought medical advice in the early stages of the disease; and a most surprising fact was that relatively so few (22) gave a history of the passage of blood. In spite of the advanced neoplastic condition of these patients our operability rate was 78 per cent.

Diagnosis

Judicious or injudicious, it is so rare that one can depend entirely upon vague abdominal symptoms to denote the presence of an early neoplasm of the colon that it seems justified, upon the slightest provocation, to employ immediately two fact-finding instruments of precision —sigmoidoscopy and radiography. Two factors are to be considered in demanding these two valuable aids in diagnosis: The first is to ease the anxiety of the patient who comes suspicious of malignancy; the second to give the physician exact information as to the presence or absence of an organic lesion. More than the mere routine barium enema should be insisted upon. The roentgenologist should *search* for the cause by means of mucosal studies of any suspicious abnormality in any segment of the colon. Numerous and repeated spot films should be taken at various angles. I re-emphasize the word "search," for by such admonition easily overlooked growths can be discovered. The many tumors of the lower sigmoid can be seen not only by the sig-

moidoscope but can be palpated by the finger in a properly conducted rectal examination.

Surgical Treatment

At the present time the treatment of nearly every disease is based upon factual findings. For instance, syphilis is treated after positive serologic tests have been made; malaria is treated after finding the plasmodium in the blood smear; pneumonia is treated only after the type has been specified; and cancer of the breast usually after biopsy and frozen section have been made.

The fundamental principles involved in the treatment of malignancy of the colon are: (1) Radical removal of the tumor and adjacent gland-bearing area; (2) Restoration of continuity of the bowel.

However, it may well be added that of almost equal consideration is the technical ability of the surgeon, the patient's condition, the pre-operative preparation of the patient.

Sixty-one of the cases herein reported were resected. Some of these were resected in the face of local extension or metastasis in the liver. There were eighteen deaths in the resected cases; there was a 29 per cent mortality. These deaths occurred in the hospital.

It is an amazing surgical commentary that although the Mikulicz operation has had heaped upon it severe criticism, yet many of the ablest surgeons have abandoned other procedures and seem convinced that the method of Mikulicz, on account of its being so eminently safe, and if properly done, adequate in the radical removal of the tumor and its gland-bearing area, is unquestionably the procedure of choice.

In the past sporadically and especially at the present time there appear enthusiastic proponents of primary resection with or without complementary decompression. This, no doubt, has resulted from an endeavor, ideal in its conception, to remove all malignant tissue and to restore bowel continuity by various aseptic techniques, over various newly invented instruments, in the shortest possible time.

Specifically, it may well be stated that for tumors of the right colon there are three suitable procedures which may be utilized, depending upon the particular lesion and complications encountered: (1) Primary resection of the colon with end-to-end, or side-to-side anastomosis. (2) A one or two-stage manoeuvre: First stage, ileo-transverse colostomy, either side-to-side or end-to-side. Second stage, extirpation of

the right colon with its tumor-bearing area. (3) Primary resection of the right colon with utilization of the Mikulicz principle of a gun barreled ileum to transverse colon as suggested and carried out so successfully by Lahey.

For tumors of the right colon I prefer a one stage procedure in the non-obstructed group, especially where we have been able to place preoperatively the distal end of the Miller-Abbott tube at or near the ileocecal valve.

The Miller-Abbott tube has proven of unquestionable benefit in decompressing the terminal segments of the small bowel in obstructive lesions of the right colon; and whether a one stage procedure or a two stage manoeuvre is carried out the use of this tube has diminished the morbidity and mortality.

The presence of this tube put down forty-eight hours prior to operation will render any operation on any segment of the colon easier, for the reason that almost the entire small bowel is telescoped over this tube into a small mass and when operating on the right colon this small mass of intestines can be placed in the left side and when operating on the left colon, especially in resections of growths of the splenic flexure, it can be placed far over in the right side of the abdominal cavity.

Tumors of the transverse colon are easily managed by an exteriorization manoeuvre, obstructive resection or resection with primary suture side-to-side or end-to-end, preferably utilizing the advantage of a complementary cecostomy.

Left sided neoplasms, particularly of the sigmoid, can be removed by a properly performed Mikulicz procedure or resection with primary anastomosis open or closed according to the site and according to the preoperative preparation of the patient. An invaluable aid in mobilization of any left sided growth is dividing the spleno-colic ligament, mobilizing and drawing down the upper splenic and descending segments.

Rankin's obstructive operation with immediate removal of the tumor mass and complementary cecostomy is undoubtedly a valuable method. The dysfuctionalization of the left bowel as advocated by Devine has been received by some in this country with enthusiasm.

Although there has been a trend to resection of neoplasms of the left side with complementary decompression and primary end-to-end

suture, I am still of the belief that with the majority of surgeons the mortality may be kept lower and an equal number of cures effected if a properly performed and adequate exteriorization or an obstructive operation is carried out with complete removal of the gland-bearing area.

I hold no brief for any one type of resection in all cases. The Mikulicz operation, in the hands of most surgeons, where the gland-bearing area is removed, is certainly safer and is equally as adequate as any type of an intestinal anastomosis. Primary resection, with side to side anastomosis, is safer, in my opinion, than any type of end to end anastomosis over clamps, or by the so-called open anastomosis. However, there are certain instances where a primary resection and immediate anastomosis is justified, especially if there is no obstruction, or if preliminary cecostomy has been carried out.

I believe that the preoperative use of certain sulfonamides such as sulfasuxadine and sulfathaldine, have helped sterilize the fecal stream. I have, however, been unable to verify the complete value of this therapy in intestinal anastomosis, for I have always used about the anastomosis, sulfanilamide crystals. Sulfa drugs as adjuvants in intestinal surgery do not take the place of meticulous and thoughtful technique, and regard for adequate blood supply.

Conclusion

From the study of this somewhat limited group of malignancies of the colon, a good many points worthy of emphasis may be noted.

1. Our effort to obtain valuable information as to early signs and symptoms was fruitless.

2. More frequent use of the sigmoidoscope and the employment of the x-ray after barium enemas is to be emphasized in patients who come with the slightest suspicion of a disturbed gastrointestinal tract.

3. Needless to say any patient undergoing an abdominal operation of any magnitude whatsoever, should be hydrated; the fluid balance maintained; electrolytes at a high level; and plasma protein within the limits of safety.

4. If the growth is in the transverse, descending, or sigmoid colon, cecostomy should be performed, and for the most part, a good piece of the cecal head should be brought out on to the abdominal wall. There is too much danger in the use of a Pezzer catheter type of cecos-

tomy.

5. If the ileocecal valve is patent, and the tumor is in the cecum and ascending colon, the intelligent use of the Miller-Abbott tube to decompress the small bowel is a great advantage. The Miller-Abbott tube will render any operation on any segment of the bowel easier if put down forty-eight hours preoperatively. For the entire small intestine can be telescoped upon it.

THE PATHOLOGIC PHYSIOLOGY OF GASTRIC AND DUODENAL ULCER*

HARRY SHAY

GASTRIC and duodenal ulcers situated as they are in different organs, nevertheless produce profound changes in function in the stomach. It is not singular that gastric ulcer causes such changes. It is not evident, however, why duodenal ulcer, a lesion beyond the stomach, should alter gastric function so often and so strikingly. It is my assignment to demonstrate the changes in gastric function produced by these lesions and to present an explanation for them compatible with the character and location of their pathology. I shall limit my discussion to uncomplicated gastric and duodenal ulcers.

Gastric and duodenal ulcers cause alterations in gastric motor and secretory functions. The changes in motor function, the roentgenologist utilizes in his diagnosis of these lesions; the alterations in secretion revealed by fractional gastric analysis, though not diagnostic, frequently yield information exceedingly helpful in clarifying the clinical picture, and in suggesting therapy. It is periodically said that the data derived from fractional gastric analyses do not justify the time consumed by the procedure. With this point of view I do not agree. It is not intended that the results of fractional gastric analysis alone be diagnostic of any disease. But, evaluated along with the rest of the clinical picture, information obtained from fractional gastric analysis more than justifies its use.

The primary x-ray signs of niche, accessory pockets, and organic hour-glass constrictions are of little interest to us for this evening's discussion, since they represent anatomic changes. Any alterations in motor function which they produce are to a great extent due to altered mechanics rather than to changed functional mechanisms. In the secondary, or indirect, signs, especially in duodenal ulcer, we see striking changes in gastric motor function that have long demanded explana-

* Lecture delivered October 13, 1943 at the Sixteenth Graduate Fortnight of The New York Academy of Medicine. From the Medical Research Laboratory, Samuel S. Fels Fund, Philadelphia.

tion. These indirect signs consist of changes in gastric motility and evacuation. The former result in hyperperistalsis and hypertonicity and the latter in rapid gastric emptying.

The spastic manifestations of incisura, spasmotic hour-glass and diffuse gastrospasm, seen in gastric ulcer, may be explained as initiated by the direct irritant action of the lesion upon the local musculature or upon related nervous structures (Auerbach's, Meissner's plexuses). A change in gastric emptying, if present in gastric ulcer, takes the form of motor delay. Except in lesions near the pylorus, this may be the result of (a) *reflex pylorospasm* and (b) *impaired gastric peristalsis* and *tonus*.

The altered gastric motor function in uncomplicated duodenal ulcer expressed by hypertonicity, hyperperistalsis, and rapid gastric emptying, does not permit of so ready an explanation. From results obtained through studies in the human subject during the past fifteen years, we believe we have come to an understanding of the mechanism which produces these altered gastric motor functions. To explain the changes, however, we should first consider certain phases of normal gastric motor activity.

The normal evacuation of gastric contents is dependent upon gastric tonus, gastric peristalsis, and the activity of the pyloric sphincter. From roentgen studies in the human subject, we[1] have concluded that the activity of the pyloric sphincter is of primary importance in gastric emptying. Thomas,[2] from studies in the dog, believes that antral activity is the chief factor in normal evacuation, an opinion shared by Quigley.[3] This difference of interpretation is not germane to our present discussion. However, the now generally accepted opinion that the duodenum houses a mechanism which exercises an influence over all three (gastric tone, peristalsis and pyloric sphincter) is vital to the development of an adequate explanation for the disordered gastric function seen in uncomplicated duodenal ulcer.

Almost invariably, modern textbooks on human physiology state that the theory propounded by Cannon, that the pylorus is controlled by acidities of the gastric and duodenal contents, has been disproven. With such statements we are not in complete agreement. The first half of the Cannon theory—that a high acidity on the gastric side of the sphincter causes the pylorus to open—has been disproven. However, the second part of the theory that an adequate acidity on the duodenal

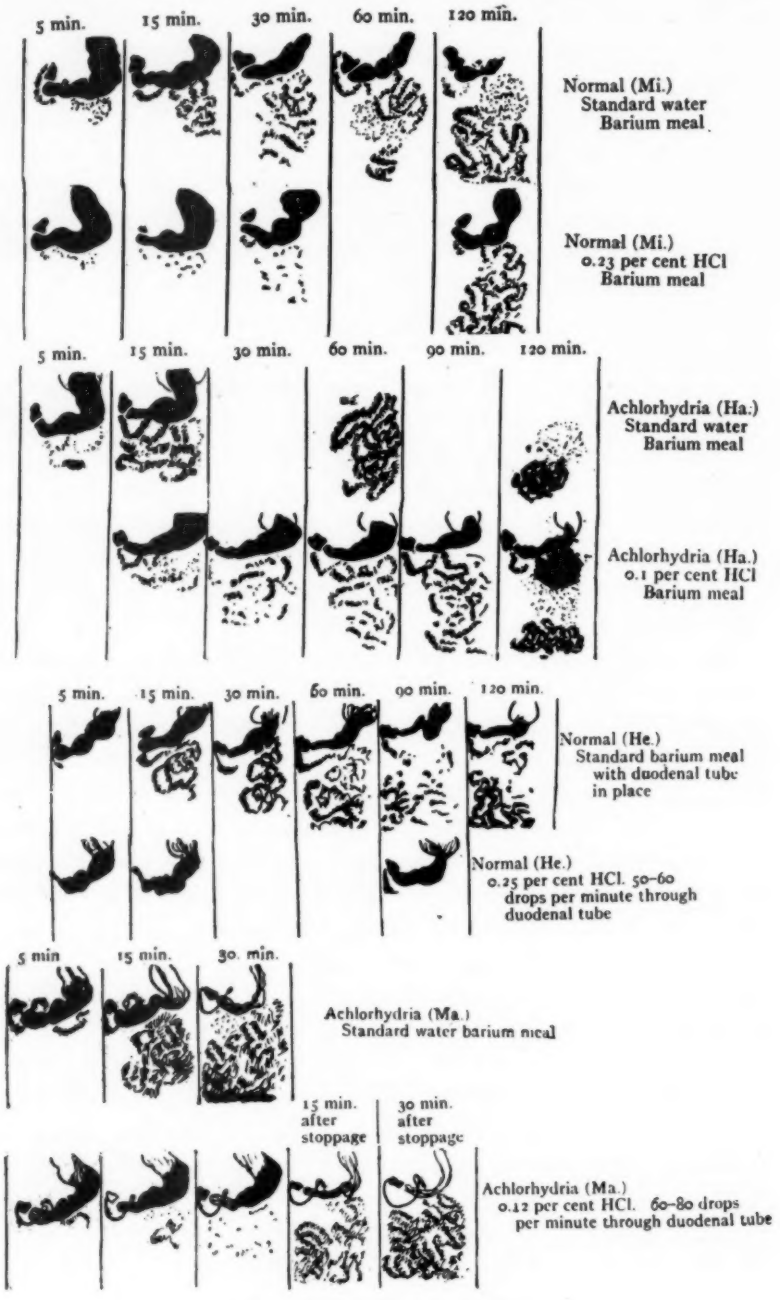


Fig. 1—Legend, see following page.

side has an ability to delay gastric empyting we[1] have been able to prove repeatedly in the human subject. This action is demonstrated if gastric evacuation of a standard meal is studied in normal individuals, and especially in achlorhydric subjects. If a person with a normal gastrointestinal tract and a normal gastric secretion is given 250 cc. of a water-barium sulphate mixture after an adequate fast period, his stomach will empty in from 60 to 120 minutes. When we repeat this study using a weak hydrochloric acid solution instead of the water, gastric emptying will be delayed. The delay in gastric emptying produced by an acid meal will be especially marked if the test subject has gastric achlorhydria. When a similar weak hydrochloric acid solution is dripped slowly into the duodenum and the test meal is administered orally, the marked delay in gastric emptying shows that the cause for these changes does not lie in an action of the acid on the gastric side of the pyloric sphincter (Fig. 1). The gastric hydrochloric acid really acts as the intrinsic agent which stimulates a duodenal mechanism concerned with the inhibition of gastric emptying. The inhibition persists until the pH of the proximal duodenum is raised to that level at which activation of the mechanism ceases. There is then further gastric empty-

Figure 1

Artists pen and ink drawings made to scale from X-ray films.

Row 1—Gastric emptying of 250 cc. water plus 2 oz. barium sulphate mixture in an individual with a normal gastric acidity response to an Ewald type meal.

Row 2—Gastric emptying in the same person when 0.23 per cent hydrochloric acid was substituted for the water. Note the considerable delay in gastric emptying produced.

Row 3—The gastric emptying of the water and barium meal in a patient with gastric achlorhydria.

Row 4—Note striking change in gastric evacuation when only 0.1 per cent hydrochloric acid was substituted for the water .

Row 5—Gastric emptying of water and barium meal in a person with a normal acid response to the Ewald type meal and a duodenal tube in place. No instillation into duodenum had been made.

Row 6—Gastric emptying of the water and barium meal in the same individual, when hydrochloric acid (0.25 percent) was instilled into the duodenum at the rate of 50-60 drops per minute. Instillation was begun with the administration of the water and barium meal by mouth. Gastric evacuation was completely inhibited. At 90 minutes when considerable gastric emptying had taken place when no duodenal instillation had been done, now showed no barium beyond the 2nd portion of the duodenum where the tip of the duodenal tube was located, through which the acid was instilled.

Row 7 and 8—Results of similar experiments performed in an achlorhydric subject. Row 8 illustrates the rapid adjustment in the duodenum when the acid instillation is stopped. With practically complete inhibition of gastric emptying, while the acid was instilled into the duodenum, gastric emptying progresses rapidly in the first 15 minutes after the instillation is stopped and is complete in 30 minutes.

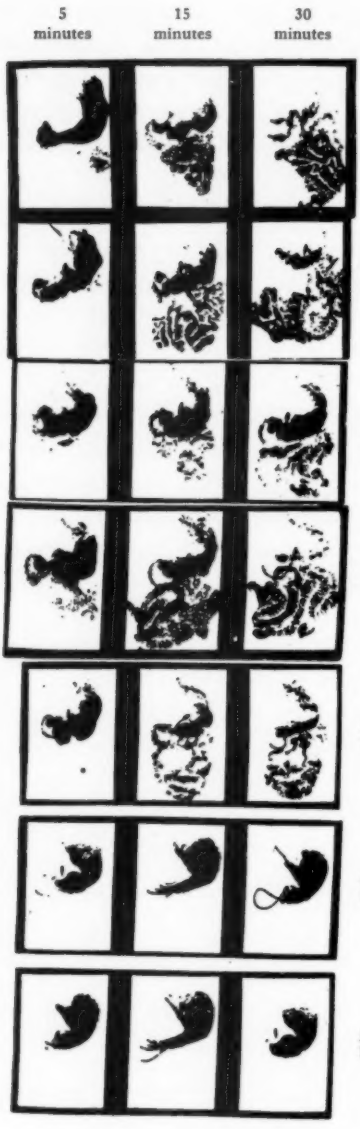

5 minutes
15 minutes
30 minutes
Water meal empty in 30 minutes.
Duodenal tube in place. Water meal empty in 30 minutes.
Tap water 80 drops per minute into doudenum. 50% residue water meal in stomach at 30 minutes.
Normal saline 80 drops per minute into duodenum. Water meal empty in 30 minutes.
5% glucose 80 drops per minute into duodenum. 10% residue water meal in stomach at 30 minutes.
40% glucose 80 drops per minute into duodenum. 100% gastric residue water meal at 30 minutes.
5% saline 80 drops per minute into duodenum. 100% gastric residue water meal at 30 minutes.

Fig. 2—Legend, see following page.

ing and the above process is repeated, resulting in the rhythmicity of gastric evacuation encountered in the normal individual.

While gastric empyting may thus be greatly influenced by the entrance of hydrochloric acid into the duodenum, we have shown and repeatedly stressed the fact that such an effect can be caused by agents other than the acid.[4] The mechanism in the duodenum may be activated by foods as well as by other substances capable of altering the physical or physico-chemical conditions in the duodenum. Delay in gastric evacuation has been produced with hypertonic solutions of electrolytes such as NaCl, $NaHCO_3$, and non-electrolytes like glucose and also by fats and fatty acids. The action of fat is particularly basic to an understanding of the prominent part played by milk and cream in the ulcer diet. Foods, however, in order to be able to activate the duodenal mechanism, must reach the duodenum in proper concentrations or in proper form. In the stimulation of the duodenal mechanism the action of the hydrochloric acid depends on the duodenal pH produced, since in hypotonic solutions it is very effective. For the action of the salts and glucose, hypertonicity of the solution is a prerequisite. This obviously does not apply to fats, since they are insoluble in water. The local physiological actions of the various substances in the duodenum may be quite different, yet the gastric motor end result is the same in each, namely, delayed gastric emptying (Figs. 2 and 3).

Figure 2

Illustrating the effect of osmotic conditions in the duodenum upon gastric evacuation. An achlorhydric subject was selected for this illustration in order to eliminate the action of the intrinsic gastric acid stimulus of the normal individual.

Row 1—Gastric emptying of standard water and barium meal.

Row 2—Emptying of similar meal with duodenal tube in place. Illustrates the failure of tube through pylorus to significantly alter gastric emptying.

Row 3—Tap water when given by mouth leaves the stomach at a rate not noticeably different from that of an isotonic solution. This is due to the fact that such a meal rapidly becomes isotonic in the stomach. Water dripped into the duodenum at the rate of 80 drops per minute causes a definite delay in gastric evacuation because of its hypotonicity, it alters osmotic conditions sufficiently to stimulate the duodenal mechanism concerned with gastric evacuation.

Row 4—Normal saline into duodenum fails to change gastric evacuation.

Row 5—The same is true when 5 per cent glucose, a nearly isotonic solution, is instilled into the duodenum.

Row 6 and 7—When hypertonic solutions of either non-electrolytes such as glucose or electrolytes such sodium chloride are instilled into the duodenum—a very striking delay in gastric emptying occurs. The delay in evacuation varies as the degree of hypertonicity of the duodenal instillate.

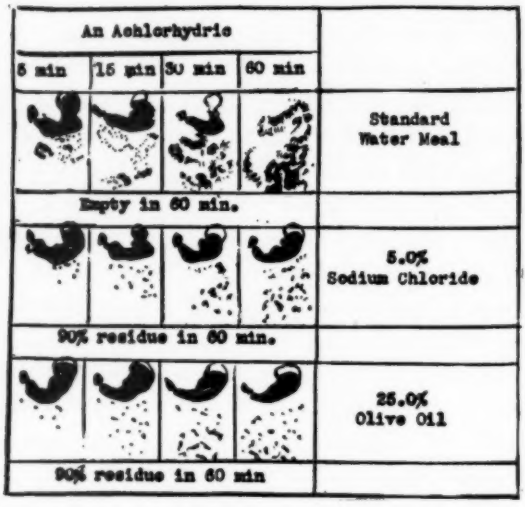
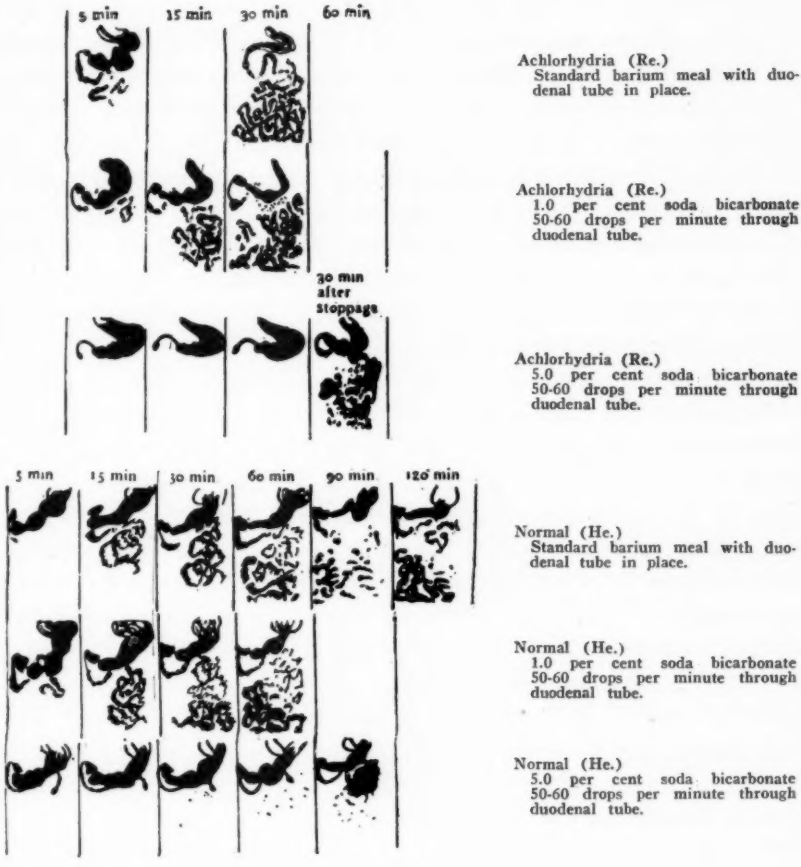


Fig. 3. Illustrating the delay in gastric evacuation when the water of the meal orally administered (Row 1) is changed to 5 per cent sodium chloride (Row 2), and to a 25 per cent emulsion of olive oil (Row 3).

When normal gastric acid is present, the regular stimulation of the duodenal mechanism is assured. When gastric acid is absent, as in the achlorhydric, the intrinsic stimulus is missing and the normal rhythmicity of gastric emptying is lost when the ingested meal does not contain a suitable stimulus. Our studies[1] with various concentrations of sodium bicarbonate demonstrate the behavior of the duodenal mechanism under various conditions. An isotonic solution of sodium bicarbonate dripped into the duodenum will influence gastric emptying of a water-barium meal, depending upon the gastric acid response of the test subject. In an individual with gastric anacidity, gastric evacuation will be unaffected by the duodenal instillate. In one with normal gastric acidity, gastric evacuation will be hastened. This occurs because the duodenal instillation of an isotonic, or nearly isotonic, solution of sodium bicarbonate, while itself incapable of activating the duodenal mechanism, actually enhances the normal neutralizing apparatus of the duodenum, hastens neutralization of the gastric contents entering the duodenum, and hurries gastric evacuation. However, when the sodium bicarbonate instilled is hypertonic, gastric evacuation is delayed in all cases (Fig. 4).



Achlorhydria (Re.)
Standard barium meal with duodenal tube in place.

Achlorhydria (Re.)
1.0 per cent soda bicarbonate 50-60 drops per minute through duodenal tube.

Achlorhydria (Re.)
5.0 per cent soda bicarbonate 50-60 drops per minute through duodenal tube.

Normal (He.)
Standard barium meal with duodenal tube in place.

Normal (He.)
1.0 per cent soda bicarbonate 50-60 drops per minute through duodenal tube.

Normal (He.)
5.0 per cent soda bicarbonate 50-60 drops per minute through duodenal tube.

Fig. 4.

The effect upon gastric emptying of a sodium bicarbonate solution administered orally or intraduodenally depends upon the concentration of the solution and the type of gastric acid response of the individual. The duodenal instillation of a 1 per cent (nearly isotonic) solution of sodium bicarbonate in an achlorhydric subject (Row 2) does not change materially the gastric evacuation of the oral water and barium meal when compared with its emptying when nothing was instilled into the duodenum (Row 1). A 1 per cent sodium bicarbonate solution does not change osmotic conditions in the duodenum of an achlorhydric sufficiently to stimulate the duodenal mechanism described.

In an individual with a normal gastric acid response, the duodenal instillation of such a solution hastens gastric evacuation (See Rows 4 and 5), because the bicarbonate enhances the normal duodenal neutralizing mechanism and so more rapidly neutralizes the gastric acid mixture reaching it intermittently through the pylorus.

The duodenal instillation of hypertonic solutions of sodium bicarbonate cause a marked delay in gastric evacuation, whether the patient is an achlorhydric or has a normal gastric acid response (See Rows 3 and 6).

The following experiment besides illustrating this point, produces conditions which indicate the fallacy of the first part of the Cannon theory of gastric evacuation. Through a tube with its tip in the proximal duodenum we slowly instilled a 5 per cent solution of sodium bicarbonate. A 0.5 per cent hydrochloric acid solution containing barium sulphate was administered by mouth. Thus, while acidity on the gastric side of the pyloric sphincter and alkalinity on the duodenal side should have been ideal for gastric emptying from the standpoint of the Cannon theory, the merest traces of barium sulphate were seen to pass the pylorus during the two hour period of observation.

In our roentgen studies in the human subject we were especially impressed with the closure of the pylorus as a result of duodenal stimulation. However, gastric peristalsis and tonus were also decreased. We[1] have pictured our concept of the local mechanism concerned in gastric evacuation in a simple simile: "The stomach is like a dumbwaiter ever ready to deliver through its door, the pylorus, anything reaching it. The duodenum, however, sensitive connoisseur, is selective. If the gastric contents are acceptable to the official taster, the duodenal cap, gastric emptying continues uninterruptedly; if not, the door, or pylorus, is hurriedly closed and stays so until the portion stated, 'trial portion,' is rendered acceptable." Quigley[3] although stressing antral peristalsis rather than pyloric action, wrote recently concerning gastric evacuation: "According to recent observations made in this laboratory, the normal course of events proceeds according to the following pattern:— A small portion of gastric contents enters the intestine. If the sample proves satisfactory, the remainder leaves the stomach rapidly; unsuitable material initiates reactions from the duodenum which temporarily retard further gastric evacuation." Thus for the major premise as it concerns our thesis for this evening, there is agreement in our findings in man with those obtained by the physiologist in dogs.

Duodenal Ulcer and Altered Gastric Motor Function: The most sensitive part of the duodenal mechanism described above is lodged in the duodenal cap. Although gastric motor function may be influenced by stimulation of the intestine beyond the cap, the sensitivity of the mechanism decreases rapidly beyond this point. In view of these findings, the clinical fact that duodenal ulcer occurs in the cap in at least 95 per cent of cases becomes especially pertinent. With the development of the ulcerative process in this area and the associated duodenitis

in adjacent portions of the duodenum, the duodenal mechanism concerned with gastric motor delay becomes impaired. Stimuli reaching the duodenum which would activate this mechanism fail to do so as readily as under normal conditions. The normal brake not acting efficiently, gastric peristalsis, tonus and gastric evacuation are exaggerated, resulting in the hyperperistalsis, hypertonicity and rapid gastric evacuation seen so frequently in uncomplicated duodenal ulcer.[5] It is important to emphasize that the duodenal mechanism is dulled only and not destroyed, because when healing of the ulcer occurs, the response of this mechanism may, and often does, become normal.

Gastric Secretion in Gastric and Duodenal Ulcer: Before discussing gastric secretion, I should like to devote a moment to a consideration of the ulcer terminology. The term "peptic ulcer" to denote both gastric and duodenal ulcer is an unfortunate one, I believe, because it makes us think of gastric and duodenal ulcers, not only as derivatives of an identical cause, but also as the producers of changes in the same physiological mechanisms. Although by definition, peptic ulcer permits grouping of gastric and duodenal ulcers, and even though pathologically both are ulcerative processes, they are quite distinct diseases in their effects on physiological mechanisms. I do not believe that physiological studies carried out in gastric ulcers should or can be applied to duodenal ulcers or vice versa. As a matter of fact it is on this basis that some of the differences of opinion in the literature can be easily understood. In general, the subject would benefit if the term "peptic ulcer" were dropped and the lesions referred to anatomically.

Hyperacidity is another clinical term for which there is no real basis, since the definitive results of Hollander[6] clearly settled the Pavlov-Rosemann Theories' controversy to establish finally that the concentration of acid in the parietal secretion does remain constant. The clinical measurement of acidity by gastric analysis measures not the acid as secreted by the parietal cells, but measures the end result of several factors—rate of acid secretion, dilution and neutralization by test meal, mucus, dilution fluid, duodenal regurgitation and also, in the case of clinical test meals, the rate of gastric emptying.

Gastric ulcer does not show a typical gastric acidity. The secretory picture, in the aggregate, is very nearly normal; however, individual gastric secretory responses, as measured by fractional gastric analysis, do vary over a wide range. This is in contrast to the usual type of gas-

tric acidity curve obtained in uncomplicated duodenal ulcer under similar conditions. The wide variation in acidities found in gastric ulcer is very probably dependent upon the location of the gastric lesion and upon the character and amount of associated gastritis. Ihre,[7] from gastric secretory studies in a large clinical material, was among the first to point out the normal rate of secretion in gastric ulcer and the hypersecretion, often marked, that occurs in duodenal ulcer. He found also that chronic gastritis without ulcer showed a clear tendency towards hyposecretion. Since there is a variable degree of gastritis associated with gastric ulcer, the interplay of reactions resulting from the location of the ulcer and the gastritis, together with the type of local response activated in the secretory cells by the pathology (ulcer destructive, gastritis-depressing), would account in good measure for the variety in acid response found in fractional gastric analyses in this disease. Support for this viewpoint may be found in the data of Vanzant, Alvarez, Berkson and Eusterman.[8] They found, from a statistical analysis of their results, that gastric acidity was below the normal level in gastric ulcer. They found a slightly greater reduction in acidity with larger ulcers (over 5 mm. dia.). Of especial interest were their findings that ulcers at, or near, the pylorus were associated with acid values not significantly different from the normal. Ulcers in the middle third of the stomach showed a reduction in acidity, while those in the upper third showed the greatest acid reduction. Differences in size could not account for a large portion of the acid producing area, therefore, only slight differences in acidity were disclosed in the data of Vanzant et al[8] dealing with this aspect of ulcers. Ulcers and associated gastritis situated in the pyloric portion of the stomach, the area whose normal secretion is alkaline, lead to no destruction or depression of acid secretory cells. Although the secretion of this portion of the stomach (containing none or only a very few parietal cells)[9] is alkaline, the rate of pyloric secretion is so low that a destructive lesion in the pyloric area appears to be unimportant to a direct control of the gastric acid picture. Apparently the pyloric mechanisms concerned with the control of the so-called second or pyloric phase of gastric secretion,[10] and with the production of the agent isolated from the pyloric mucosa by Komarov[11] which produces a high acid, low pepsin juice on intravenous injection, are not seriously impaired. This is in accord with clinical experience. The clinical observation reported by Bockus[12] that the acid titer in persons with

ulcer in the pyloric canal probably does not differ from that found in duodenal ulcer patients may have as its explanation a disturbance of the duodenal mechanism to be described under duodenal ulcer. It may result from the extension of the irritation beyond the pyloric ring producing a duodenitis and a depression of the duodenal mechanism concerned with the control of gastric secretion.

If the lesions are situated in the corporic or fundic portions of the stomach, acid producing areas are destroyed and depressed, depending on the total area involved by the ulcer and the associated gastritis. There is also evidence that local damage to the vagi may be an important contributory factor to the production of the gastric secretory depression.

Although generally it is believed that the parietal cells are distributed nearly uniformly in the body and fundus, the greater depression of acidity seen by Vanzant et al[8] in fundic over corporic ulcers, suggests the possibility of a richer distribution of parietal cells in the more cephalically located portions of the stomach.

Schiffrin and Ivy[13] in a very recent publication discussing the physiology of gastric secretion particularly as related to ulcers, commented on the hypersecretion in duodenal ulcer uniformly reported. They stated that there is no satisfactory explanation of this phenomenon. We believe our data[5] do permit a satisfactory explanation, because they account not only for a part of the mechanism concerned with the normal gastric acid curve, but also allow an interpretation of the altered curve in uncomplicated duodenal ulcer as well as a fuller understanding of the beneficial effects produced by the chief constituents of the ulcer diet.

To avoid any misinterpretation, let me emphasize that I am not suggesting that any type of gastric secretory curve is to be considered diagnostic of any disease. Nevertheless, the hypersecretory curve of gastric acidity continually rising until the stomach is empty of the test meal (Fig. 5, Curve 2), occurs so frequently in uncomplicated duodenal ulcer that the need for its explanation becomes imperative if we are to complete the picture of the altered gastric function.

Bockus, Glassmire and Bank[14] reviewed their results of fractional gastric analysis in 200 patients with duodenal ulcer and found an acidity that was higher than normal. Vanzant et al[8] from a statistical analysis of their data reported similar results although their observations were based on a single one-hour extraction after an Ewald type

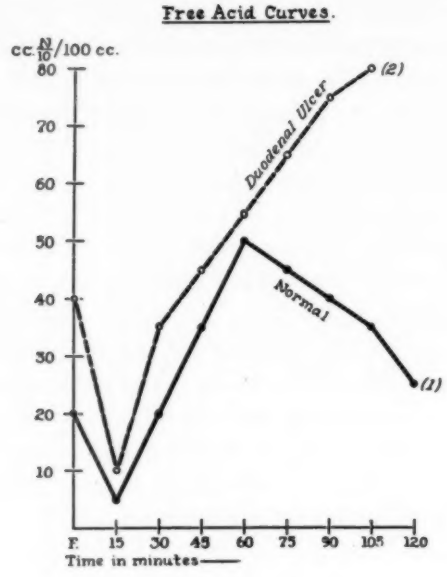


Figure 5

meal. Their results showed a mean acidity increase over normal of 12.3 units in men and 11.5 units in women. If the peak acidities of the usual continually rising type of fractional gastric acid curve had been recorded and analyzed, I believe these differences would have been even greater.

In order to attempt an explanation of the mechanism responsible for the type of gastric acid curve so frequently obtained in uncomplicated duodenal ulcer, we will first have to consider the mechanisms responsible for the gastric acid curve seen in the normal individual in response to an Ewald type test meal.

The fasting gastric contents of a normal person will show a free acidity of approximately twenty clinical units. When an Ewald type meal is administered and extractions made at fifteen-minute intervals, the acid curve usually presents the following pattern: The first fifteen-minute extraction on titration will show an apparent drop in acidity as compared with the fasting sample. This drop is only apparent and is dependent upon the dilution of the gastric contents by the test meal. This may be proven by the use of a dilution indicator.[15] After

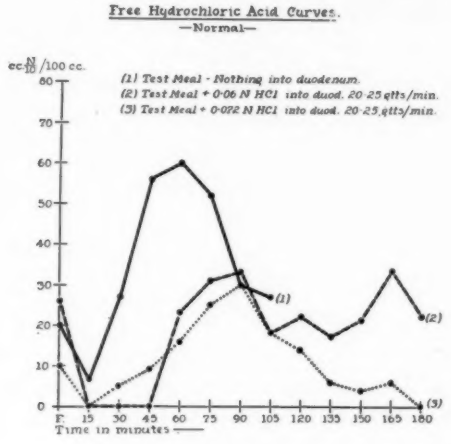


Fig. 6

For this and subsequent illustrations of gastric acid response, the following technique was used:

The patient, after an overnight fast, was intubated with two Rehfuss tubes. The tip of one was allowed to *enter the duodenum* and advance to the proximal portion of the second duodenal segment by the usual technique. The tip of the second tube was allowed to reach the most dependent portion of the stomach. The tube tips were located fluoroscopically and the tubes were fixed with adhesive about the mouth.

Curve 1—Ewald type test meal administered orally, nothing introduced into duodenum. Peak free acidity reach—60 cc. N/10 HCl per 100 cc. gastric juice (60 clinical units).

Curve 2—Free acid curve when similar test meal was given and HCl 0.06N (60 cc. N/10 HCl per 100 cc.) was dripped into duodenum at rate of 20-25 drops per minute. Note the marked depression of the gastric acidity curve under these conditions.

Curve 3—Experimental conditions same as for curve 2, but concentration of acid used was 0.72N, the peak acidity reached by the total acid during standardization for Curve 1. Curves 2 and 3 show the effect upon gastric motility as well as upon acidity —the result of stimulation of the duodenal mechanisms concerned with these gastric functions by the acid solution in the duodenum.

the first fifteen-minute extraction the acidity rises and reaches a peak at sixty to seventy-five minutes of 40 to 60 clinical units. From this point the curve takes a downward course until the stomach is empty which is usually at the end of two hours for the Ewald type meal. At this point the acidity has approximated the fasting level (Fig. 5, Curve 1).

The rising limb of the gastric secretory curve can be explained by the combined action of the cephalic and pyloric mechanisms of secretion as well as the diminishing effect of dilution by the test meal. The descending limb is, we believe, dependent upon a mechanism that is located beyond the pylorus. We base this belief upon the following evidence: If in an individual with a normal gastric acid curve

after an Ewald meal, hydrochloric acid of a concentration represented by the peak gastric acidity reached in response to that meal is dripped slowly into his proximal duodenum, the gastric acid response to a similar meal administered simultaneously will be markedly depressed (Fig. 6). Recently Friedman, Pincus and Thomas[16] in Pavlov pouch dogs found that the intraduodenal instillation of hydrochloric acid inhibits gastric secretion in response to a meal if a threshhold level of duodenal pH is attained. Particularly relevant to our concept is their finding that the threshhold level of intestinal pH for inhibition of gastric secretion is within the pH range of the antral contents. These results, we believe, prove that the duodenum in both dog and man houses a mechanism which when activated can cause a depression of gastric acidity. Further, this mechanism can be activated by an acid reaction in the proximal duodenum and this reaction can be produced by the gastric acid reaching the duodenum. In the individual with a normal duodenum, the activation of this mechanism occurs with the entrance into the duodenum of the peak gastric acidity reached for the test meal employed and accounts for the downward limb of the gastric curve seen in the normal fractional gastric analysis. The threshhold of response of this mechanism determines, we believe, in a large measure, the type of gastric acid curve the individual will show. Thus, if the duodenal mechanism is activated by a duodenal pH produced by a gastric free acidity of 40 to 60 clinical units, a normal gastric acid curve will result. However, if the threshhold of response of the duodenal mechanism is lower and responds at a higher pH, (lower acidity), gastric secretory depression will occur more readily and a low gastric acid response to the test meal will result. On the other hand, a duodenal mechanism with a higher than normal threshhold of response, one requiring a lower duodenal pH (higher acidity) to activate it, will not react until the gastric acid has reached a peak which is higher than normal response and that individual will show a hypersecretory gastric acid curve. In the variations of the threshhold of response of this duodenal mechanism lies the explanation for the isosecretory, hyposecretory and hypersecretory gastric acid responses of normal persons.

In duodenal ulcer, the lesion situated almost invariably in the cap, the location of the most sensitive part of the duodenal mechanism concerned with gastric secretion, impairs the activity of the mech-

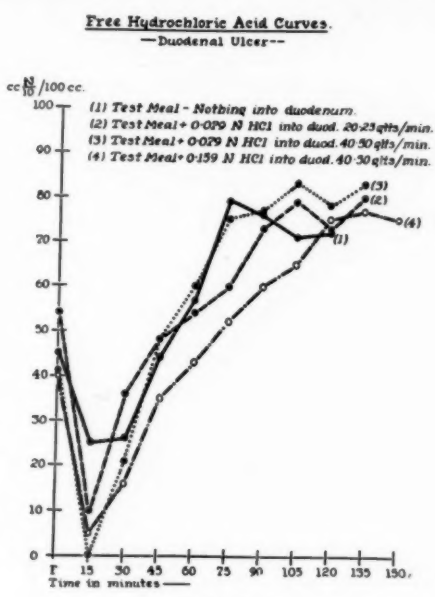


Fig. 7

Experimental conditions the same as for Fig. 6. Illustrates the continually rising type of gastric acid curve usually seen in uncomplicated duodenal ulcer (Extragastric type). It shows the failure of the duodenal mechanisms concerned with gastric motility and secretion to respond to acid representing the peak acidity reached by the patient in response to the test meal. The duodenal mechanisms are so obtunded that they fail to respond to acid instillation of increased concentrations (Curve 4).

anism to such a degree that with an Ewald type meal, the peak gastric acidity reached is usually inadequate to activate the obtunded duodenal mechanism. This is shown in Fig. 7. Such a concept would explain the results of Vanzant et al who found that smaller or single duodenal lesions caused a lower increase in gastric acidity than did larger or multiple ones. Large or multiple lesions not only involve more of the duodenal mucosa but the associated duodenitis would be greater resulting in an involvement of more of the mechanism concerned with gastric secretion. That the mechanism is dulled and not destroyed is shown by the fact that with healing, gastric acid response can return to normal (Fig. 8). The tendency for gastric acidity to moderate in

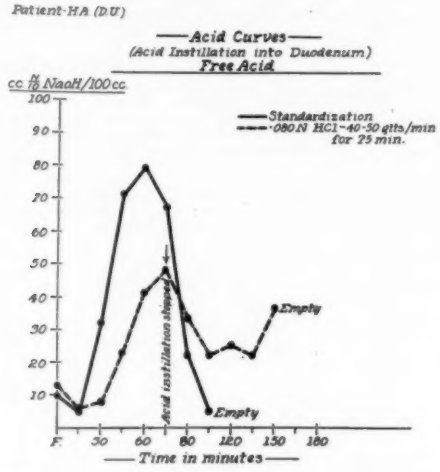


Fig. 8. Recovery of the duodenal mechanisms when ulcer healing had occurred. Same patient as in Fig. 7. Results obtained when patient had been entirely symptom free for a period of ten months. Although the peak acidity reached was not different from that seen during period of ulcer activity (Fig. 7), the type of curve had returned to normal and we could see a return of response of the duodenal mechanisms concerned both with gastric motor and secretory function.

duodenal ulcer as the gastrointestinal tract returns to normal has been reported by Brown and Dolkart.[17] Hurst[18] expressed the opinion that the characteristic x-ray findings of a hypertonic rapidly emptying stomach in duodenal ulcer and the hypersecretory hyperchlorhydric gastric curves reported by Crohn[19] were not due to the ulcer because the same phenomena could be observed after the ulcer had healed. Before accepting this view, the question of when is a duodenal ulcer healed is not impertinent, because I believe there are no reliable clinical criteria upon which such an opinion can be based. The relief of symptoms or changes in the duodenal deformity roentgenographically cannot be accepted as conclusive evidence of healing. A return of normal gastric motor and secretory functions indicates healing of the ulcer because this expresses a restoration of normal function to the proximal duodenum. If this is true, then the corollary is that a failure to restore such function is an indictment of the medical management genuinely to heal duodenal ulcer. The high incidence of recurrences

in duodenal ulcer does not make such an indictment unreasonable. The major cause for such failure is that thus far a direct attack on the disturbed physiology has not been possible. Whether there is a distinct ulcer preventive factor as the work of Sandweiss and his associates[20] suggest, has not yet been confirmed.

The results we obtained have led to the belief in our laboratory that the increased gastric acidity stands in a consequential and not in a causal relationship to the initial duodenal lesion. The development of the duodenal ulcer interferes with the normal duodenal mechanism that is concerned with the control of gastric acidity—the normal brake impaired, gastric acidity increases. This would also explain the failure of Brown and Dolkart[17] to observe any significant trend in the gastric acidity prior to a recurrence of ulcer activity. If the duodenal ulcer had not been previously healed to a degree which had permitted the duodenal mechanism to function, the acidity would, naturally, be increased during the remission, as well as during the attack. If prior to the attack there had been sufficient healing to permit proper functioning of the duodenal mechanism, gastric acidity could have returned to a normal pattern but would not have shown a change until the breakdown of the duodenal lesion had again impaired the duodenal mechanism. Our results lend significance to the isolated report of Lino.[21] After producing a lesion of the duodenal mucosa by abrasion, Lino found an increased gastric acid response to a test meal. The acidity increased to the 5th or 6th day postoperatively and then rapidly diminished to return to normal by the 8th or 9th day. Because of the autopsy results on his animal, Lino related the period of hyperacidity to the presence of the duodenal lesion, while the return to normal gastric acidity was associated with healing of the duodenal abrasion. Berk, Rehfuss and Thomas[22] have found that the contents of the duodenal bulb are more acid in patients with duodenal ulcer than in normal subjects. The rapid emptying of a hypersecreting stomach resulting from the altered duodenal mechanisms in duodenal ulcer could contribute much to the production of their findings.

We are in complete accord with Schiffrin and Ivy[13] who do not believe that gastric acidity can cause duodenal ulcer but do ascribe to the action of the acid and pepsin an important role in the chronicity of ulcer. In this connection, due emphasis must be placed upon the pepsin whose maximum activity is dependent upon an optimum pH,

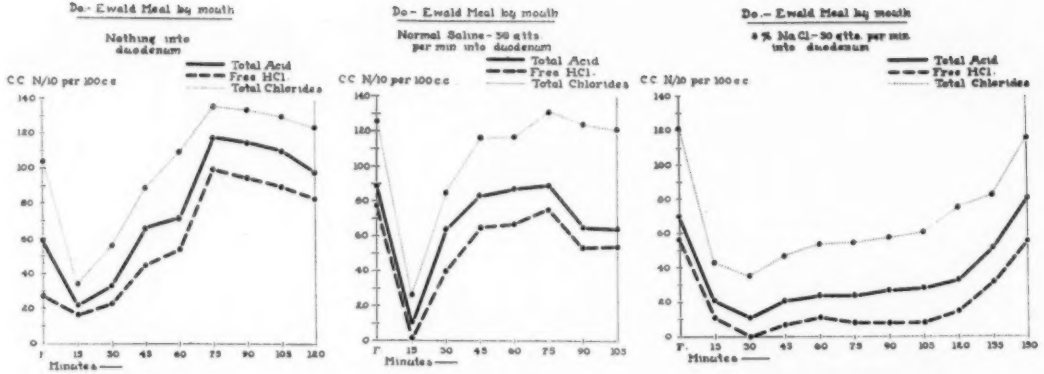

Do.- Ewald Meal by mouth
Nothing into duodenum
Do.- Ewald Meal by mouth
Normal Saline - 30 c.c. per min. into duodenum
Do.- Ewald Meal by mouth
5 % Na Cl - 30 c.c. per min. into duodenum
Total Acid
Free HCl.
Total Chlorides
CC N/10 per 100 c.c.
Minutes

Fig. 9

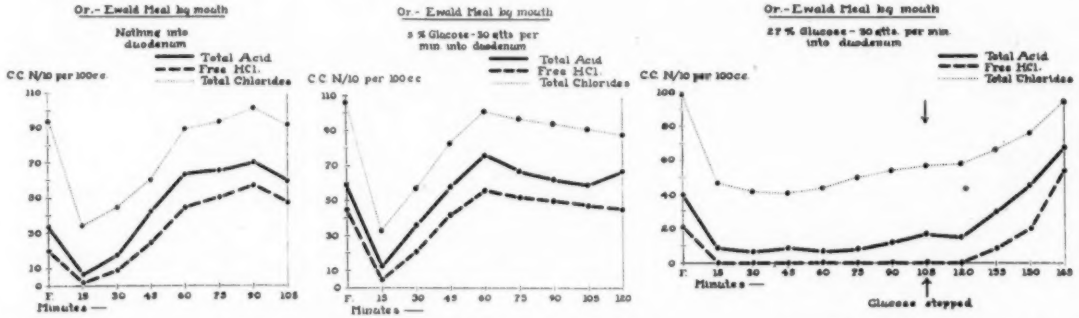

Or.- Ewald Meal by mouth
Nothing into duodenum
Or.- Ewald Meal by mouth
5 % Glucose - 30 c.c. per min. into duodenum
Or.- Ewald Meal by mouth
27 % Glucose - 30 c.c. per min. into duodenum
Total Acid
Free HCl.
Total Chlorides
CC N/10 per 100 c.c.
Minutes
Glucose stopped

Fig. 10

Fig. 9 shows the effect of alterations in osmotic conditions in duodenum upon gastric acidity. Isotonic solutions of electrolytes incapable of chemically activating the duodenal mechanisms, fail to influence gastric motor or secretory functions. Hypertonic solutions, however, stimulate these mechanisms very actively.

Fig. 10. The effect of solutions of non-electrolytes. Illustrates the influence that ingested foods may have upon gastric motility and secretion, aside from their intragastric effects, if they reach the duodenum in proper concentrations.

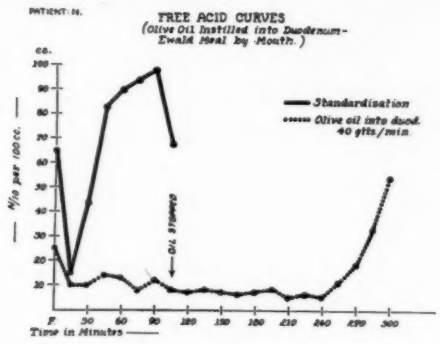


Fig. 11

The striking effect produced by the duodenal instillation of oil. Oil and cream may be effective in stimulating the duodenal mechanisms even during the active stage of duodenal ulcer. Oil instillation started with the ingestion of the Ewald type meal.

which in turn is dependent upon an adequate amount of hydrochloric acid. Schiffrin[23] has demonstrated the difference in the irritating properties of acid and acid pepsin by the perfusion of jejunal loops. Perfusion with acid pepsin solution always caused ulceration, while hydrochloric acid solution alone causes some destruction of the villi but without ulceration.

Like the duodenal mechanism concerned with the control of gastric emptying, the mechanism involved in gastric secretion is not activated solely by the gastric hydrochloric acid. Foodstuffs and other substances that reach the duodenum which have the proper chemical or physicochemical effect may do so as well.[24] Thus hypertonic solutions of electrolytes (Fig. 9) and non-electrolytes (Fig. 10), and especially fats (Fig. 11) are effective.

In our studies we[24] succeeded in showing that the major, if not the sole, action resulting from the stimulation of the duodenal mechanism was an inhibition of the nervous phase of gastric secretion since we were able to inhibit the gastric secretory response incident to the hypoglycemia produced by insulin (Fig. 12). Direct stimulation of the parietal cells appears to be unaffected by the activity of the duodenal mechanism. This was shown when duodenal stimulation failed to prevent a rise in gastric acidity after histamine was injected (Fig 12).

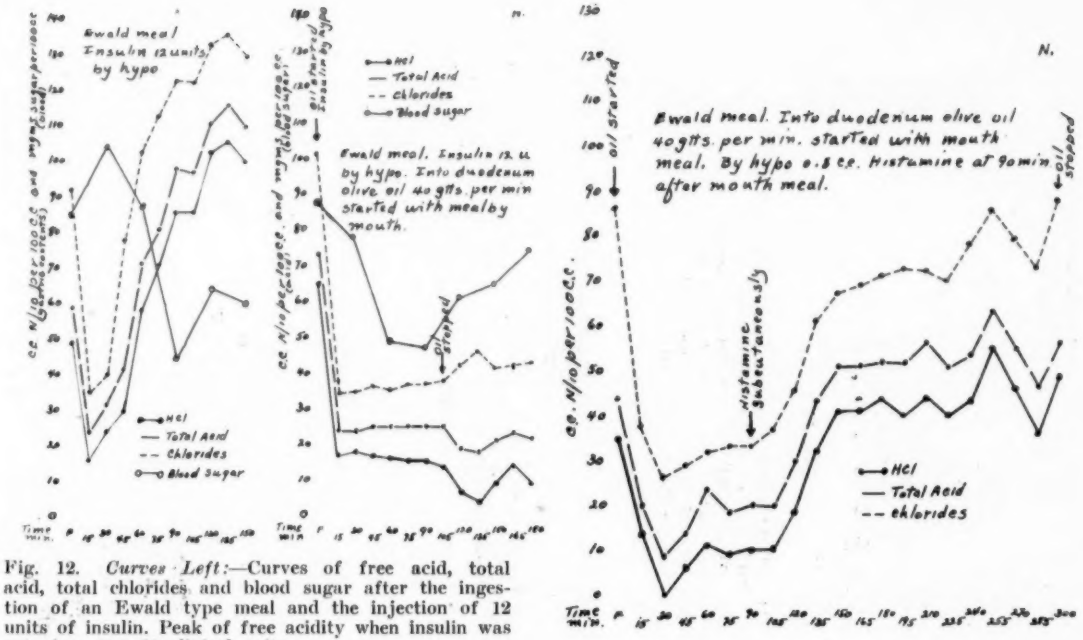

Ewald meal
Insulin 12 units by hypo
HCl
Total Acid
Chlorides
Blood Sugar
Ewald meal. Insulin 12 u by hypo. Into duodenum olive oil 40 gtts. per min started with meal by mouth.
Oil started
Oil stopped
Ewald meal. Into duodenum olive oil 40 gtts. per min. started with mouth meal. By hypo 0.8 c.c. Histamine at 90 min after mouth meal.
Histamine subcutaneously
Oil started
Oil stopped
HCl
Total Acid
chlorides
Time min.

Fig. 12. *Curves Left:*—Curves of free acid, total acid, total chlorides and blood sugar after the ingestion of an Ewald type meal and the injection of 12 units of insulin. Peak of free acidity when insulin was not given was 80 clinical units.

Curves Center:—Response of same individual under similar experimental conditions, when olive oil was instilled into the duodenum, started when the Ewald meal was taken.

Since it is established that the stimulation of gastric secretion by insulin is a central vagus effect incident to the hypoglycemia produced, the inhibition of the gastric secretion by the oil in the duodenum shows that stimulation of the duodenal mechanism described, influences the nervous or first phase of gastric secretion.

Curves Right:—Ewald meal given, olive oil instilled into duodenum. After 90 minutes when the duodenal effect of the oil on the gastric acid curve was clearly established, histamine 0.1 mg. per 10 kilo of body weight was injected subcutaneously. Even though the duodenal instillation of the oil was continued, a sharp rise in gastric acidity soon occurred. Direct stimulation of the parietal cell, an effect which histamine action represents, is therefore not prevented by stimulating the duodenal mechanism.

Since vagal secretion is rich in pepsin, an impairment of the duodenal control mechanism would explain the hyperpepsinia as well as the hyperacidity reported in duodenal ulcer by Ihre.[7]

In the rather extensive literature on gastric secretion during sleep, all observers agree that during heavy sleep secretion is practically in abeyance in normal people but Winkelstein[25] found in duodenal ulcer cases that free secretion continued throughout the night. This was confirmed by Henning and Norpoth.[26] Considering these findings it is pertinent that Day and Webster[27] were able to demonstrate in dogs that gastric secretion, stimulated through the parasympathetic nervous system or by the presence in the intestine of food substances and products of their disintegration, is inhibited by the introduction of hydrochloric acid into the duodenum. An impairment of this duodenal mechanism could, therefore, explain the frequent clinical observation of a high interdigestive secretion in duodenal ulcer. It would explain also the high basal secretion reported by Bloomfield, Chen and French[28] as well as their failure to find such increased secretion in gastric ulcer.

The modus operandi of the duodenal mechanisms for gastric motor and secretory functions we are not prepared to state. There is evidence that both nervous and humoral mechanisms are involved. If the action is dependent upon the production of enterogastrone we do not know, although Gray, Bradley, and Ivy[29] have shown that enterogastrone containing preparations extracted from the upper intestine, inhibits both gastric motility and secretion. Our results in the human being differ from those of Gray et al in that they found that their extract was effective in inhibiting the secretory response of dogs with pouches to histamine. We were unable to check histamine secretion in the human subject by stimulating the duodenal mechanism. Friedman, Pincus and Thomas[16] were able to confirm in Pavlov pouch dogs that insulin-provoked secretion is inhibited by an adequately acid duodenal content, but that histamine-provoked secretion is not.

The duodenal mechanisms concerned with gastric motor and secretory functions react at different levels of stimulation. The one concerned with gastric motor function responds at a lower level than does the one which influences gastric secretion. This illustrates nature's logical procedure, because it is desirable at the beginning of a meal that gastric emptying be slowed to allow for proper gastric mixture and digestion, while gastric secretion should be depressed later only

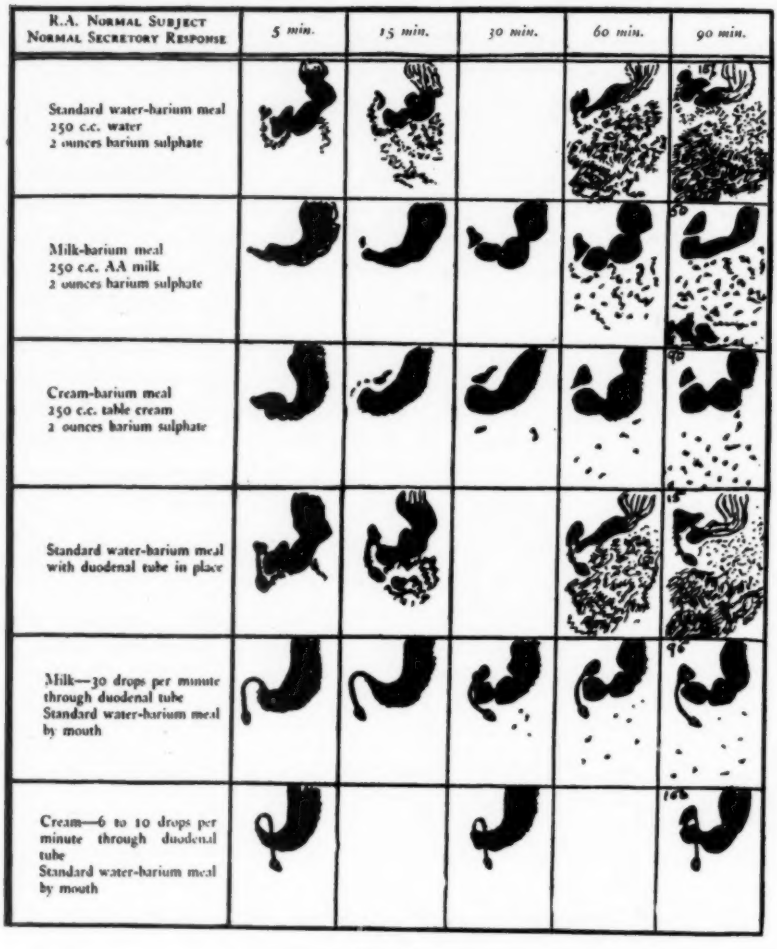


Fig. 13

Striking inhibition of gastric emptying produced by milk and cream. Rows 5 and 6 show this effect to be due to the action of these substances in the duodenum.

when these have been accomplished.

Having considered the mechanisms involved in the production of the disordered gastric motor and secretory function in gastric and duodenal ulcer, it may not be amiss to consider briefly how these disturbed functions are altered by ulcer therapy. Milk and cream have been and remain the mainstays of the ulcer diet. Data have gradually

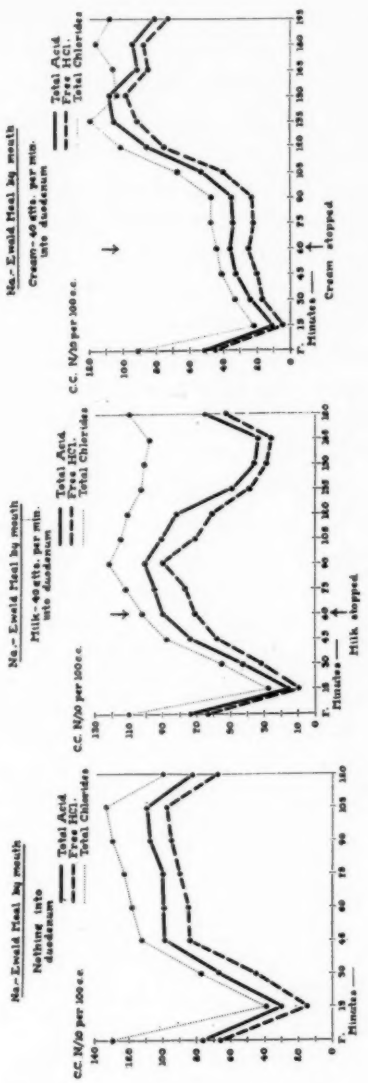


Fig. 14

The center curves show that milk in the duodenum depresses gastric evacuation but does not appreciably influence the gastric acid curve. The duodenal instillation of cream, however, stimulates both duodenal mechanisms, the one concerned with gastric secretion, as well as that which influences gastric evacuation. The effects of milk and cream (Figs. 13 and 14) may be obtained in patients with active duodenal ulcer. In this action, we believe, rests an important part of the major role maintained by milk and cream in the ulcer diet.

accumulated to show why this should be. If gastric hydrochloric acid and pepsin are important in the chronicity of ulcer, neutralization of acid and binding of pepsin become of paramount importance. For this purpose milk is an ideal food; its protein will bind pepsin and its buffer action in neutralizing acidity has been amply demonstrated.[30] Milk has the further advantage that as a gastric stimulant it calls forth

a very low rate of gastric secretion with the lowest acid and pepsin values in comparison with other common foods.[31] When to these effects is added the action of fat in the duodenum,[32] the special value of cream becomes evident (Figs. 13 and 14). In the difference of the effect of milk and cream upon the motor and secretory functions of the stomach may also be seen what is meant by the difference in threshhold of response of the duodenal mechanisms concerned with gastric motor and secretory functions. I have already pointed out that the duodenal mechanisms concerned with gastric motor and secretory functions are dulled, *not* destroyed, in most instances in duodenal ulcer. It is true also that the action of fats is more effective than that of gastric acid in stimulating these mechanisms—we have been able to produce a response by fats in ulcer patients when acid failed.[33] In this action lies an important part of the beneficial value of milk and cream and fat to the ulcer diet. It may be, too, that those uncomplicated duodenal ulcer patients who fail to respond to a medical regime may represent cases of duodenal mechanisms which have been so damaged that they fail to react even to fat. In these cases the diet and medication would be unable to restore normal gastric function even in part and thus fail to relieve the subjective symptoms of pain and distress which are manifestations of the disordered gastric physiology.

Summary

1. Gastric and duodenal ulcers produce changes in gastric motor and secretory functions.
2. The changes caused by the former can be related to the action of the lesion upon local gastric mechanisms.
3. The changes in gastric function produced by duodenal ulcer, we believe, we have demonstrated to be due to damage of duodenal mechanisms, whose activities are concerned with decreasing gastric evacuation and secretion.
4. The most sensitive portion of these duodenal mechanisms is located in the cap, the usual site of duodenal ulcer.
5. As a rule, the mechanisms are obtunded and not destroyed by the ulcer and may recover with healing of the lesion. A return of gastric motor and secretory function to normal, we offer as probably the only reliable criteria of healing of a duodenal ulcer.
6. Though obtunded by the ulcer and associated duodenitis, the duo-

denal mechanisms in most cases of active ulcer can still respond to stimulation by fat. Upon this fact, rests part of the therapeutic value of milk and cream in the ulcer diet.

7. An impairment of the duodenal mechanisms to a degree where they can not react even to fat stimulation may account for those uncomplicated duodenal ulcers that fail to respond to a medical regime.
8. The duodenal mechanism concerned with gastric secretion, we believe, is largely responsible for the diminishing gastric acidity seen in the second half of a normal fractional gastric analysis and is an expression of the self-regulatory mechanism of gastric secretion.
9. The term "peptic ulcer" is an undesirable one because gastric and duodenal ulcers are not derivatives of the same cause and in their effects upon gastric physiological mechanisms they are different diseases, in spite of the fact that they are both ulcerative processes.

I am aware that I have not discussed other mechanisms that may influence gastric motor and secretory functions. I thought I could perhaps be most useful, if I were to crystallize for you what we have learned about the local gastric motor and secretory mechanisms from their study directly in the human subject and how that information might be used to explain the manifestations of disordered gastric function with which we as clinicians are constantly confronted in the management of patients with gastric and duodenal ulcer.

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PRIMARY ATYPICAL PNEUMONIA IN GENERAL HOSPITALS AND IN PRIVATE PRACTICE*

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and

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THE reports on primary atypical pneumonia of unknown etiology or so-called "virus-type pneumonia" that have appeared in increasing numbers during the past five years have described this disease as it has occurred among special groups of individuals such as in colleges,[1, 2] army camps,[3, 4] and among medical and nursing personnel of hospitals,[5] but very little has been written about its occurrence in general hospitals or in private practice. The explanation for this is clear. Primary atypical pneumonia of unknown etiology as seen in college infirmaries or in army and navy station hospitals stands out as a well-defined disease entity, whereas in general hospitals and in private practice with patients of all ages included, the cases of primary atypical pneumonia are intermixed with such a variety of other respiratory cases that it is difficult to visualize the disease in its pure form. The clinical diagnosis of primary atypical pneumonia in private practice and in general hospitals usually is difficult and sometimes impossible, whereas in the special groups mentioned the diagnosis is obvious even in the early stage of the disease.

Our experience with pneumonia started at Bellevue Hospital, where nearly all of the pneumonias were proved bacterial infections and where we saw only an occasional primary atypical pneumonia, although in retrospect we believe that each year there were some atypical cases, particularly among the late summer and early fall pneumonias that were milder and gave an unsatisfactory pneumococcal typing. Next, we had experience at The New York Hospital and in private practice

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in New York City, where we observed more of the primary atypical cases. Since the introduction of sulfapyridine a large part of the consulting pneumonia practice in New York City has dealt with the primary atypical disease. Finally, during last fall and winter (1942-1943) we were given the opportunity to follow and study 205 pneumonia patients hospitalized in the Cornell University Infirmary in Ithaca, N. Y., of whom 196 were adjudged to have the primary atypical variety. This last experience gave us our first picture of the disease in its almost unadulterated form and furnished us a basis for comparison with our earlier experiences with pneumonia.

Fortunately, the clinician now is attaining a clearer conception of the different etiological varieties of pneumonia. We know now that in addition to the recognized bacterial pneumonias (pneumococcal, streptococcal, staphylococcal, etc.) there are also, but much more rarely, rickettsial pneumonias (typhus, Rocky Mountain spotted fever, and Australian and American Q fever) and true virus pneumonias (psittacosis, ornithosis, and possibly influenza and others). In addition, there is a pneumonia that has many clinical resemblances to the proven rickettsial and virus pneumonia which we now designate as primary atypical pneumonia, etiology unknown.

Until recently this disease was designated by a different name in almost every report dealing with it. The following list shows the maze of terminology that was used:

Virus pneumonia
Virus-type pneumonia
Primary virus pneumonitis

Interstitial virus pneumonia
Interstitial virus pneumonitis

Acute interstitial pneumonia (pneumonitis)
Acute interstitial pneumonitis

Pneumonitis
Acute pneumonitis
Simple pneumonitis

Atypical pneumonia
Primary atypical pneumonia
Atypical pneumonitis
Atypical pneumonia with leukopenia

Atypical bronchopneumonia of unknown etiology
Bronchopneumonia in adolescence
Bronchopneumonia of unknown etiology
Bronchopneumonia of unknown etiology (variety X)

Acute influenzal pneumonitis
Acute influenzal pneumonia

Disseminated focal pneumonia
Benign broncho pulmonary inflammation associated with transient radiographic shadows

Primary atypical pneumonia, etiology unknown

It can be seen that the tendency has been to use pathological as well as etiological terms. Still today the pathology as well as the etiology of this disease is almost completely unknown because of the few fatalities that have occurred from it. (Perhaps a better designation would be "primary atypical pneumonia, etiology *and pathology* unknown.") To call this disease influenzal pneumonia or influenzal pneumonitis is particularly misleading, because this terminology already is used to designate three other types of pneumonia: the 1918 variety which was rapidly fatal and probably a secondary bacterial infection following influenza, the pneumonia caused by the influenza bacillus or Pfeiffer's bacillus, and the true virus pneumonia caused by the influenza virus. Until more is known about the etiology and pathology of primary atypical pneumonia, a clinical terminology only should be used. It is even true that the disease may not be primarily a pneumonia, but a more general infection in which the pulmonary changes are only of secondary importance, such as in typhus or Q fever.

Atypical pneumonia, as we have observed it at the Cornell University Infirmary and as it has been described as occurring there[2] and in other colleges and in army camps, certainly seems to be a well defined

disease entity, and its incidence in special groups and also in general practice is relatively high. As in pneumococcal pneumonia, this pneumonia of unknown cause varies in its incidence from year to year. Last year (1942-43) its incidence was high; this year (up to the present) it has been much lower. Each year since this disease has been recognized, its prevalence has been high in the late summer and autumn and much lower in the winter and spring, the time when the incidence of pneumococcal pneumonia is the highest. We clinicians believe that this seasonal relationship should give the epidemiologists some clue to the mode of transmission of this type of pneumonia. This year another unusual phenomenon occurred which may offer some lead as to the origin of this disease. About November 20, when influenza A appeared in this section of the country, primary atypical pneumonia almost entirely disappeared.

We believe it to be true that primary atypical pneumonia is occurring in every part of the United States, probably in every part of the world. Reports from our own army station hospitals have described cases in almost all parts of the U. S., as well as in the Hawaiian Islands, Panama Canal Zone, the South Pacific area, Europe, and North Africa. In civilian practice, primary atypical pneumonia is widespread and has become one of the more important medical diseases. Every hospital in New York City last year, and this year to a less extent, has seen a number of cases of this disease. Last year on the infectious disease service of The New York Hospital there were 29 cases of primary atypical pneumonia as compared with 47 of pneumococcal lobar pneumonia. In the entire hospital there were 52 cases during the year. The disease occurs at every age and in every walk of life. Our oldest patient at The New York Hospital was sixty-six and our youngest was four years of age. Persons in early adult life are apparently much more frequently afflicted, as evidenced by the high incidence of the disease in universities and in army and navy camps. The incidence among physicians and nurses is high. The medical departments of industrial organizations are diagnosing many mild cases of the disease by taking chest x-rays of employees who are returning to work after a number of days at home because of so-called "grippe" or a chest cold.

We call this disease atypical pneumonia. Nevertheless, it has a number of striking clinical characteristics and in some respects its course is more typical than that of lobar pneumonia. The onset is rarely sud-

den, such as that of the chill or the severe pleural pain of lobar pneumonia, but is gradual and frequently insidious. Fever, with associated chilly sensations, headache and generalized weakness, usually initiates this type of pneumonia. Because the fever is intermittent—and this is one of its chief characteristics—it is sometimes not discovered for several days. Shortly after the onset a dry, irritating cough commences, although some patients exhibit no cough throughout their illness while in others it is a very distressing symptom. Late in the disease the cough becomes productive of a small amount of mucopurulent sputum; but occasionally the expectoration is profuse. The sputum is almost never rusty and tenacious (so-called "pneumonic"); however, occasionally associated with severe coughing it may be slightly blood-streaked. The patient quite often complains of a slight to moderate soreness in the chest but almost never has real pleural pain. The appearance of the patient presents a striking contrast to that seen in pneumococcal pneumonia. At the time of day when the temperature is elevated, the skin may be moist and flushed, but only the severe cases show any degree of cyanosis or dyspnea. The average duration of fever is 9 days, but we have observed patients in whom it has persisted for more than 6 weeks and others in whom it lasted less than 24 hours.

The physical signs in primary atypical pneumonia usually are not very helpful in making the diagnosis. In a few early cases and in most of the late ones, rales can be heard over the affected lung but as a rule the signs are not sufficiently pronounced to present an accurate criterion of diagnosis. The breath sounds may be suppressed in the early stages. A few cases (less than 10 per cent) have signs of consolidation.

The x-ray findings have been more helpful than any other in accurately diagnosing and in shaping our present concept of primary atypical pneumonia. The earliest change is that of increase in the bronchovascular markings extending from the hilum, changes which sometimes can be made out only by having for comparison an earlier normal film. Soft homogeneous shadows develop later along these distended roots, and finally a fan-shaped density extends into the periphery. Occasionally either a homogeneous lobar shadow or a bronchopneumonic type of mottling, resembling a tuberculous infiltration, is found. In a few early cases the first x-ray was negative and was not positive until the third or fourth day of the disease. This is one of the evidences that suggests the disease is a generalized one; perhaps in only part of

the cases does it localize in the lung. At any rate, today it is impossible to diagnose this infection without a positive x-ray examination.

One of the most remarkable features of primary atypical pneumonia is the frequency with which all of the routine laboratory tests, other than the chest x-ray, are negative. One may see a patient with a temperature of 104°F. with extensive x-ray signs, and still the blood count, urine analysis, blood culture, sputum examination, throat culture, and even a variety of serological studies are all negative. The blood count early in the disease is usually within normal limits, except for possibly a slight increase in the young polymorphonuclear cells. During the later stages of infection the total white cell count usually is slightly elevated and we have occasionally seen, late in the disease, an elevation up to 25,000. The negative sputum examination and negative blood culture study are most important confirmatory findings in this disease. Careful and complete bacteriological studies always should be carried out in any severe case in which there is concern about the final outcome. Special virus studies, except in a few cases, have not been at all revealing. The identification of the causative agent of atypical pneumonia remains a most active field for investigation. Many reports have appeared but, except for a very few cases proven to be caused by known viruses or rickettsia, the disease as a whole continues to be of unknown etiology.

The serum of patients recovering from primary atypical pneumonia is positive for cold agglutinins in a high percentage of cases.[6] Also in some patients the convalescent serum shows heterophile antibody. Recently Horsfall and his coworkers[7] have reported that during convalescence they have obtained a positive agglutination test, using a specific strain of streptococcus isolated from a case of primary atypical pneumonia. None of these tests is specific, and while a positive finding with one of them may occasionally offer some confirmatory evidence in diagnosis, the particular interest in them seems to be in the clue that these findings may offer for discovering the causative agent of this pneumonia.

Before discussing treatment, I shall present a few case records in order to emphasize the clinical characteristics of primary atypical pneumonia. Chart I is of a patient having a moderate or mild course, the type of case that makes up almost 90 per cent of those seen. This girl, aged 20, was admitted to the Cornell University Infirmary on January

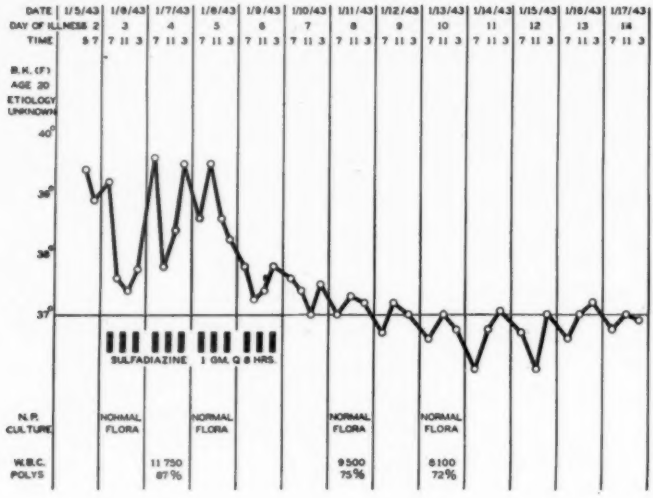

Chart. I. Mild case of primary atypical pneumonia, etiology unknown.

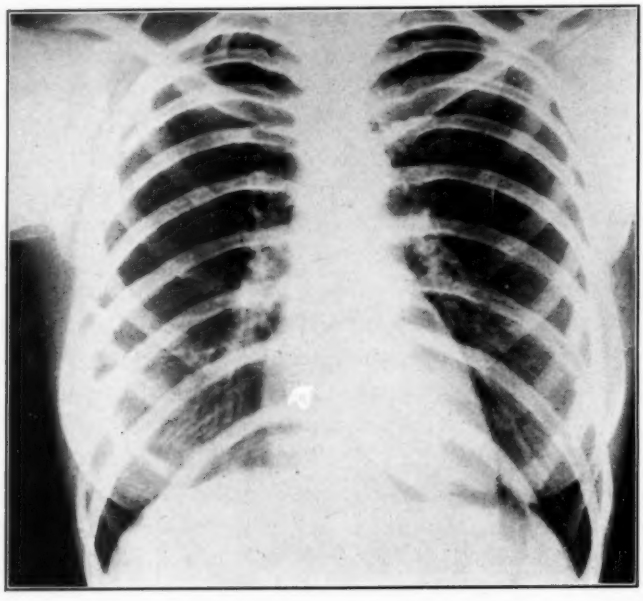

Figure 1. Chest x-ray taken on second day of illness in mild case of primary atypical pneumonia (Chart I). It shows a small area of light productive infiltration in the right base.

5, 1943, with a history of fever, chills, headache, and a general aching for one day. She had had symptoms of a "cold" for 2½ weeks. Physical examination revealed slight congestion of the upper respiratory tract and rales over the right lower lobe. The blood on January 7 contained 11,750 white cells, 87 per cent being polymorphonuclear cells. Chest x-ray (Fig. 1) was reported by Showacre of the Cornell Infirmary as showing a "small area of light productive infiltration in the right base." A diagnosis of primary atypical pneumonia was made.

The patient ran a moderately high intermittent fever for 4 days and then recovered by rather rapid lysis. She received sulfadiazine 1 Gm. t.i.d. for 4 days as part of an investigation, and it was believed not to have influenced the course of the infection. Nasopharyngeal cultures on January 6, 8, 11, and 13 showed only the usual flora. Special serologic studies for influenza virus identification were made by Thomas M. Magill but were negative.

With very few variations this case is being seen over and over again today. The diagnosis of primary atypical pneumonia is made by:

1. Gradual onset with chills, fever and cough.
2. Relatively high intermittent fever in a patient usually exhibiting very little cyanosis or dyspnea and no pleural pain.
3. A white blood cell count, usually within normal limits.
4. Positive chest x-ray.
5. Negative bacteriological studies.
6. No response to sulfonamides.

The next is a severe case of primary atypical pneumonia (Chart II). Fortunately for the doctor, only about 10 per cent are of this type, because they always present serious diagnostic and therapeutic problems. This patient was a girl, aged 19, admitted to Cornell University Infirmary on January 28, 1943, with a history of fever, chills, cough, headache, and pain behind the eyes for 2 days. Physical examination revealed slight congestion of the upper respiratory tract and slight dullness and rales over the left lower lobe. She appeared rather sick, had a flushed face, and a tight irritative cough. The white blood count was 13,500 with 88 per cent polymorphonuclear cells. On January 29, a chest roentgenogram showed a "slight irregular thickening of the pulmonic markings along the left heart border," and on January 30 there was a "definite area of linear infiltration in the left base along the left heart border." A diagnosis of primary atypical pneumonia was made.

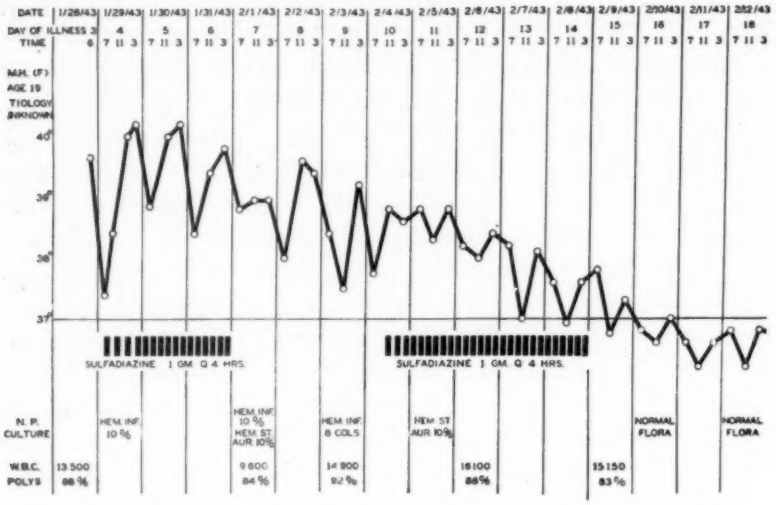

Chart II. Severe case of primary atypical pneumonia of unknown etiology.

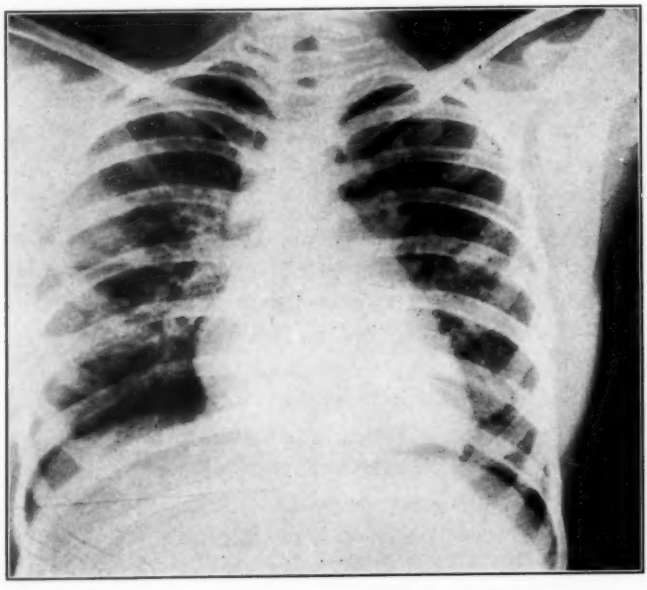

Figure 2. Chest x-ray taken on tenth day of illness (Chart II) in a severe case of primary atypical pneumonia and showing extensive mottling throughout both lung fields.

Sulfadiazine 1.0 Gm. every four hours was commenced shortly after admission, chiefly because serious bacterial infection could not be ruled out. This was discontinued after 3 days because there was no response. On February 4 there were physical signs of spread into the right lung, the roentgenogram (Figure 2) showed "diffuse interstitial infiltration throughout the lower two-thirds of the left lung field and all of the right lung field except the apex, with scattered confluent 1-2 cm. areas in the outer third of the right lung," the white blood cell count was 14,900, and the nasopharyngeal culture showed Hemophilus influenzae and hemolytic Staphylococcus aureus. Because of these findings, sulfadiazine was started again and was continued for the ensuing five days, during which time the temperature dropped slowly to normal. Eventually recovery was complete clinically and by x-ray, although follow-up physical examinations revealed rales over the left lower lobe for two months.

In cases such as this one, the doctor will not be very secure as to the diagnosis or outcome until a specific diagnostic test is discovered. A high white count, which some authorities believe portends a more rapid recovery, and the finding of potential pathogens in the respiratory tract, which always suggests secondary invasion, confuse the picture of primary atypical pneumonia. We believe that response to the second course of sulfadiazine in this patient was more apparent than real. Response to sulfonamide therapy is more abrupt, as a rule.

The following case (Chart III) is that of an apparently genuine virus or psittacosis pneumonia. This patient, a 52-year-old woman, had had malaise, chills, fever, headache, and cough for 6 days before admission to Bellevue Hospital. On admission she was very much distressed by the cough and headache, but did not appear critically ill. There were many coarse rales and slight impairment of breath sounds over the right base. The sputum showed no significant organism. The leukocyte count was normal and remained so in spite of a high, irregular febrile course. There was no response to a 3-day course of sulfathiazole. Sulfadiazine given in the second week, however, may have exerted an influence on the infection. The x-ray (Figure 3) made on the 9th day of illness showed an extensive bronchopneumonia, much more prounounced on the right side. In this case there had been contact with pigeons, and six of eight birds examined had complement-fixing antibodies. The patient's serum in the second week showed a positive

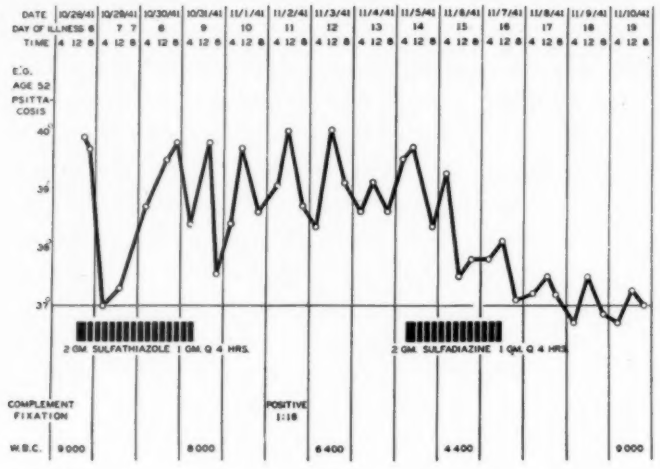

Chart III. Psittacosis pneumonia with severe course and recovery.

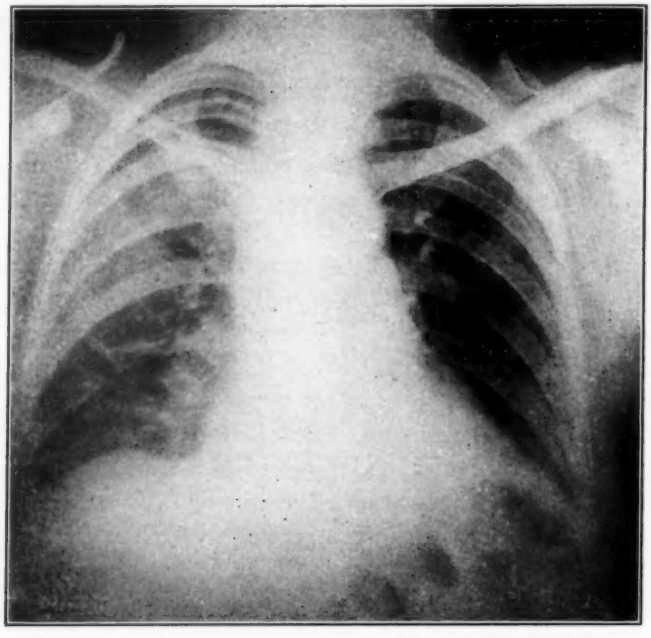

Figure 3. Chest x-ray made on ninth day of illness in a case of psittacosis pneumonia (Chart III).

complement fixation in a dilution of 1 to 16, and at a later time after full recovery, it was positive in a dilution 1 to 128. This apparently is a proven virus pneumonia, and its resemblance to the virus-type of the disease or primary atypical pneumonia is readily recognized.

The next case (Chart IV) shows a fatal psittacosis pneumonia in a 44-year-old woman, who was admitted after five days of illness and who died on the thirteenth day. No elevation of the white blood count was recorded until the day before death. The complement fixation test was positive in a dilution of 1 to 64 of serum. A virus identified as a member of the psittacosis group was isolated from the lung tissue.* The chest x-ray (Figure 4) taken shortly after admission to the hospital shows consolidation in the middle third of the right lung field. This x-ray film is not particularly different from that seen in pneumococcal pneumonia. Also it suggests cancer of the lung.

Finally we wish to present one case (Chart V) in contrast to those already included. This young man, aged 20, was admitted to the Cornell University Infirmary on January 4, 1943, with a history of a mild cold for about two weeks, followed by fever, headache, cough, and general aching for one day. He appeared acutely ill on admission and showed marked congestion of the upper respiratory tract, slight suppression of breath sounds and a few rales over the right lower lobe. The blood contained 24,000 white cells, 93 per cent polymorphonuclears. Chest x-ray (Figure 5) revealed a "small area of acute productive infiltration in the right cardiophrenic angle." The appearance of the x-ray in this case, the onset, and the fact that at the time there were thirty or more cases of primary atypical pneumonia in the Infirmary, all weighed strongly in favor of this latter diagnosis. However, an excellent rule to be remembered in such cases is: "When in doubt, use sulfonamide." Sulfadiazine was given 2.0 Gm. initially and then 1.0 Gm. q. 4 hours. After a high temperature spike to 41°C. a few hours after admission, there was a critical drop in temperature and rapid recovery. One of the two small post-critical rises in temperature may have been related to a remittance of sulfonamide therapy. Subsequent repeated nasopharyngeal cultures showed first a pure culture of pneumococcus Type 7, and then pneumococcus 7 and Hemophilus influenzae. The acuteness and severity of illness, the high white count on admission, and particularly

* The virus studies in the two psittacosis cases were carried out by Joseph E. Smadel and Louis Thomas of the Rockefeller Institute, and we are also indebted to Sarah Flanders of Bellevue Hospital for her efforts in completing the work-up of the Bellevue cases.

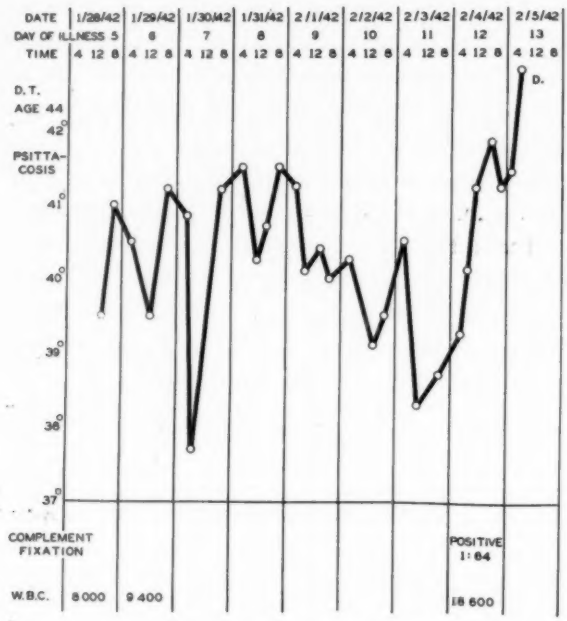

Chart IV. Fatal case of psittacosis pneumonia.

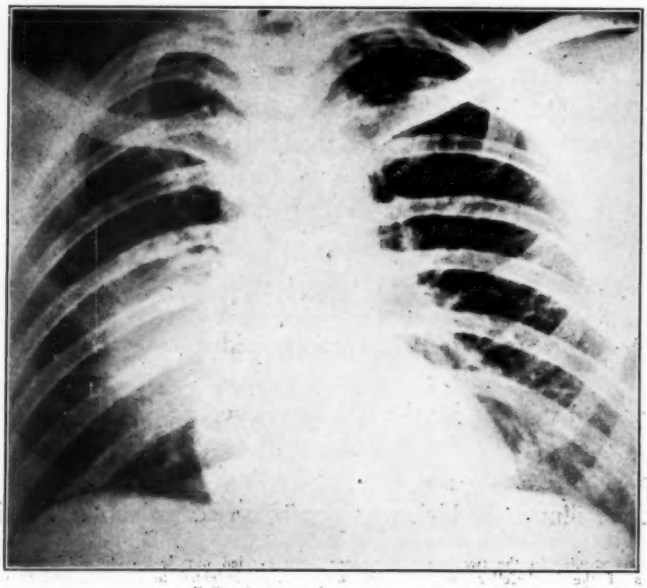

Figure 4. Chest x-ray on sixth day of illness in a fatal case of psittacosis pneumonia.

the rapid response to sulfadiazine are decided contrasts to the course and findings in the virus-type cases. Serious mismanagement occurs in these cases if sulfonamide therapy is withheld or delayed too long.

Primary atypical pneumonia enters the differential diagnosis of almost every respiratory infection. The milder cases commonly pass as influenza or "grippe" or "chest or grippy cold." The protracted cases must be distinguished from tuberculosis, bronchiectasis, and even carcinoma of the lung. The differentiation between primary atypical pneumonia and tuberculous pleurisy or any disease where there is a small pleural effusion can be very difficult. Recent reports that show bronchiectasis, pleural effusion and empyema as complications of primary atypical pneumonia must be evaluated very carefully, because in reality the suspected complications may represent the primary disease. A grave error is to mistake pulmonary infarct for primary atypical pneumonia, but the most serious mistake of all is to label a case of progressive pneumococcal infection as primary atypical pneumonia and to withhold specific therapy until it is too late to be effective.

The present treatment of primary atypical pneumonia is of about the same order as was the treatment of all pneumonia in the time of Sir William Osler. "It is a self-limited disease, which can neither be abated nor cut short by any known means at our command . . ." Furthermore, one should heed his counsel: "We should bear in mind that patients are more often damaged than helped by the promiscuous drugging which is only too prevalent."

We have already indicated in our discussion that the number one problem in treatment is *accurate and careful diagnosis*. Only a very few diagnostic procedures are necessary in the mild, transitory case (although we doubt that anyone can be accurate in diagnosing this disease without using the x-ray routinely). However, in the acute or severe case a large number of diagnostic procedures, particularly careful bacteriological studies, must be carried out and in a systematic way.

The second consideration is that of *wisely using or not using the sulfonamides*. Now it can be stated that primary atypical pneumonia per se is rarely ever benefited by the sulfonamides. Furthermore, proven secondary bacterial infection in this disease has been uncommon. The elevated white blood cell count late in the disease does not necessarily indicate secondary infection, but is probably a phase of the hemogram of this particular disease. In addition, finding a higher type pneumo-

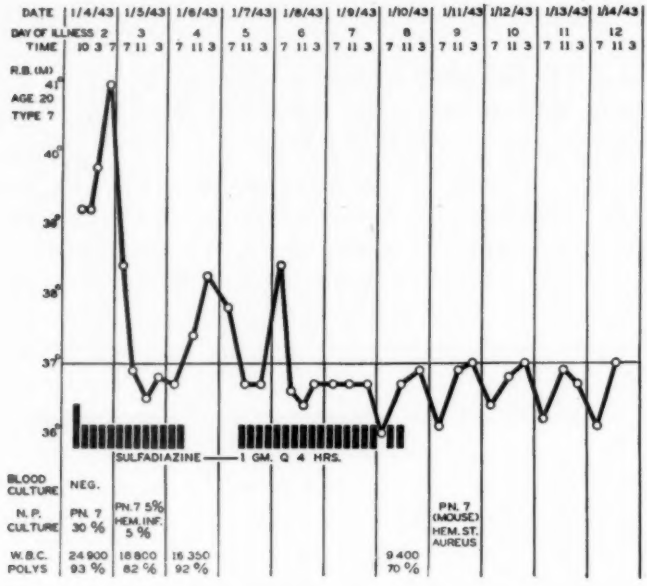

Chart V. Type 7 pneumococcal pneumonia.

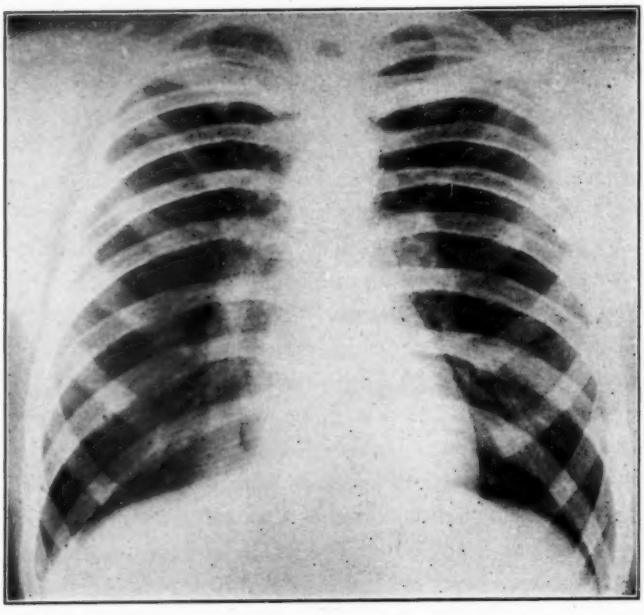

Figure 5. Chest x-ray in case of Type 7 pneumococcal pneumonia. Its appearance is very similar to that frequently seen in primary atypical pneumonia.

coccus or even a hemolytic streptococcus in the sputum does not mean that there is a secondary infection. What are the practical applications of this knowledge? We believe that on this basis the mild case is best treated *without* sulfonamide. However, the severe or doubtful one should receive a trial of the drug because of the danger of a mistaken diagnosis or a secondary infection, even though the latter has been rare. The trial should last not more than 3 or 4 days, during which time the dosage should be sufficient to insure a blood concentration of 5 to 10 mg. per cent. Sulfadiazine in our experience has proven to be the drug of choice, but should always be administered with sufficient alkali to keep the urine neutral or slightly alkaline. In a limited clinical trial, penicillin has been found to have no effect upon the course of atypical pneumonia.

The next consideration is a *judicious symptomatic and supportive therapy*. In this respect again we should divide the cases into the mild and severe. The mild one as a rule needs no treatment except rest and proper nursing care. The severe case, on the other hand, needs much attention and can tax every medical resource available. Oxygen, transfusions, and infusions occasionally are required. The cough, with chest soreness and general restlessness, is the most common symptom-complex. Here the physician can fully exercise the art of medicine and frequently he can control a serious situation by such simple measures and considerations as proper room ventilation, a chest binder, electric pad, oil of eucalyptus rubbed on the chest, or the use of a simple, nonirritating cough mixture. A few patients require sedatives, codeine, codeine and papaverin, or morphine; and when such treatment is indicated, it must not be postponed too long. The symptomatic treatment of severe cases of atypical pneumonia could be detailed at great length, but in the end it must be individualized both for the patient and the physician.

Finally, just as in the army with the soldier and the home folks, *the morale of the patient and his family is very important*. In a disease such as primary atypical pneumonia, which has a low fatality rate and rare complications but in which the course may be severe and protracted, the physician should be particularly generous with encouragement and explanation. This will be a most important part of the therapy of this disease until medical science evolves a specific etiology and therapy.

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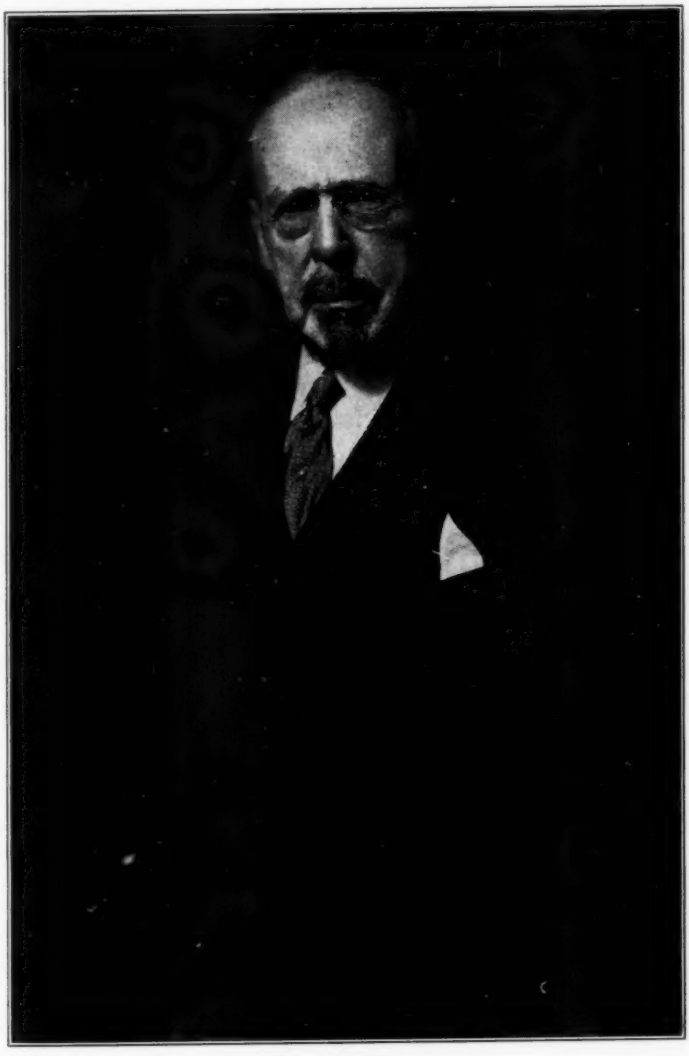

BERNARD SACHS
1858-1944

IN MEMORIAM

Bernard Sachs

We come here, all of us, with love and reverence to take leave and bid God-speed to a dear friend.

You have known him, so I can add little to what you know. You have been familiar, for perhaps scores of years, with his erect sturdy form, with his quick step, instinct with drive and purpose.

His light shone before men, and always to lead them and make easier their footsteps; and it shone the world over, wherever doctors met and talked together.

He radiated an old Roman Virtus—as I once said, one could not stand with him for ten minutes in shelter from a shower and not perceive in him an uncompromising honesty and a forceful goodness.

His rare hesitations in speech or action came only from his fear that he might wound in inadvertence. A gentleman is said to be one who never hurts anyone unintentionally, and Barney Sachs could and did fight doughtily for his idea of the right against wrong-thinking and wrong-doing, but never, in most of a life-time did I know of his being careless to a friend or colleague—indeed often he suffered some foolish ones overlong.

His friends knew his wisdom and his honour; many bequeathed to him burdens and great charges to be furthered when they themselves had left the scene of their endeavors, and we know the scruple and keen effort he used to make the aims of those good friends live on among men.

No honour was missing: to that within himself were added all those that could be given to one of our Profession; he was twice President of the American Neurological Association, President of the Academy of Medicine, and as President of the International Neurological Con-

gress, he made American Medicine refulgent in Europe. To all these, and to duties to his City, and to his pursuit of literature, he brought distinction of conduct and of word: but also, to each task he brought an immense energy which sprang, I know, from a great and unfailing love for his fellow man—a love which, with his skill, cured and assuaged the sick, and comforted the afflicted.

He loved, he toiled, he served, he *led*,
"Nothing is here for tears, nothing to wail
or knock the breast; no weakness, no contempt,
Dispraise or blame; nothing but well and fair,
And what may quiet us in a death so noble."

FOSTER KENNEDY

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("Possession does not imply approval.")

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PROCEEDINGS OF ACADEMY MEETINGS

STATED MEETINGS

FEBRUARY 3—*The New York Academy of Medicine Stated Meeting.* ¶ Executive Session. Reading of the Minutes. ¶ Papers of the Evening. Indications for and Value of Psychotherapy from the Practitioner's Standpoint. —a] The indications for psychoanalytic therapy, Franz G. Alexander, Professor of Psychiatry, University of Illinois, College of Medicine. b] Psychotherapy in general practice, S. Bernard Wortis, Lucius N. Littauer Professor of Psychiatry, New York University College of Medicine. ¶ Report on Election of Fellows.

FEBRUARY 17—*The Harvey Society in affiliation with The New York Academy of Medicine.* The Fifth Harvey Lecture, "The Circulation in Traumatic Shock in Man," Dickinson W. Richards, Jr., Associate Professor of Clinical Medicine, College of Physicians and Surgeons, Columbia University.

SECTION MEETINGS

FEBRUARY 1—*Section of Dermatology and Syphilology.* ¶ Presentation of Cases—a] From The Mount Sinai Hospital. b] Miscellaneous Cases. ¶ General Discusion. ¶ Executive Session.

FEBRUARY 4—*Section of Surgery.* ¶ Reading of the Minutes. ¶ Presentation of Cases —a] Megacolon—bilateral lumbar sympathectomy—one year follow-up, Louis R. Kaufman, Metropolitan Hospital. b] Advanced hypertension — thoracolumbar sympathectomy—one and one-half year follow-up, J. William Hinton, Post-Graduate Hospital. c] Essential hypertension — Peet operation — eight and one-half year follow-up, Frederic W. Bancroft, Fifth Avenue Hospital. d] 1. Raynaud's disease of upper extremity — cervical sympathectomy — six month follow-up. 2. Raynaud's disease of upper extremity—multiple anterior rhizotomies — two year follow-up. 3. Immersion foot—lumbar sympathectomy—eight month follow-up. 4. Hyperhidrosis — lumbar sympathectomy—two year follow-up, Bronson S. Ray, New York Hospital. ¶ Papers of the Evening—a] Physiology of the autonomic nervous system, Donal Sheehan, New York University College of Medicine (by invitation); b] The surgery of the sympathetic system, Captain James C. White, MC-V (S) USNR, Chelsea Naval Hospital, Boston (by invitation). ¶ General Discussion. ¶ Executive Session.

FEBRUARY 8—*Section of Neurology and Psychiatry and the New York Neurological Society.* ¶ Papers of the Evening—a] Disturbances in sleep mechanism, Charles Davison, Captain Edwin L. DeMuth (by invitation); Discussion, Samuel Brock, Henry A. Riley; b] Narcolepsy as a psychogenic symptom (case report), Leo A. Spiegel, C. Philip Oberndorf; Discussion, Samuel Brock, S. P. Goodhart; c] Sequelae and complications in shock therapy, S. Eugene Barrera (by invitation), B. L. Pacella (by invitation); Discussion, S. Bernard Wortis, Hubert S. Howe. ¶ General Discussion. ¶ Executive Session.

FEBRUARY 10—*Section of Pediatrics.* ¶ Reading of the Minutes. ¶ Presentation of Cases. ¶ Papers of the Evening. Pediatrics and the War—a] The Emergency Maternity and Infant Care Program—A federal plan for aiding Service Men's families, Leona Baumgartner; b] The effects of wartime conditions on infectious diseases of children, Ernest L. Stebbins; c] Juvenile delinquency and the war, Dudley D. Shoenfeld. ¶ General Discussion. ¶ Executive Session.

FEBRUARY 15—*Section of Medicine.* ¶ Reading of the Minutes. ¶ Papers of the Eve-

ning (*Fifteen minutes each*)—a] Cardiac manifestations due to allergy, Joseph Harkavy, Mt. Sinai Hospital; b] Clinical and chemical results of castration for metastatic prostate carcinoma, Alexander B. Gutman, Presbyterian Hospital; c] Vitamin studies in peripheral vascular failure, A. Wilbur Duryee, Ellen McDevitt, A.B. (by invitation), Bertrand Lowenstein (by invitation), Post-Graduate Hospital; d] Varices of the bronchial veins as a source of hemoptysis, John E. Deitrick, New York Hospital. ¶ Discussion led by William S. Tillett. ¶ Executive Session.

FEBRUARY 16—*Section of Genito-Urinary Surgery.* Order: ¶ Reading of the Minutes. ¶ Paper of the Evening—Operative indications in benign and malignant disease of the prostate (*slides and motion pictures*), Hugh H. Young, Johns Hopkins Hospital (by invitation). ¶ General Discussion—George F. Cahill, Roy B. Henline, Joseph F. McCarthy, Alexander R. Stevens. ¶ Executive Session.

FEBRUARY 16—*Section of Otolaryngology.* ¶ Reading of the Minutes. ¶ Presentation of a New Instrument—Pharyngological Photoelectric Colorimeter, Samuel J. Kopetzky. ¶ Papers of the Evening—a]Congenital laryngeal stridor (Inspiratory laryngeal collapse) (*motion pictures*), Leo Schwartz; b] Radiation and surgery in the treatment of tumors of the hard palate and nasal sinuses, G. Allen Robinson. Discussion, Andrew A. Eggston, John M. Lore; c] Treatment of certain forms of deafness, tinnitus and dizziness by means of benzyl cinnamate. (Cases presented), Jacob Jacobson (by invitation). Discussion, Samuel J. Kopetzky.

FEBRUARY 18—*Section of Orthopedic Surgery.* ¶ Reading of the Minutes. ¶ Presentation of Cases—a]Osteoid—osteoma of the lumbar spine *From the Hospital for Joint Diseases,* Francis B. Roth (by invitation); b] Scoliosis in twins, Frederick Vom Saal (by invitation). ¶ Papers of the Evening—a] Plantar flexed talus, Frederick R. Thompson. Discussion opened by Alan DeForest Smith; b] Hemifusion in tuberculous joints, John R. Cobb. Discussion opened by David M. Bosworth. ¶ Executive Session.

FEBRUARY 21—*Section of Ophthalmology.* ¶ Instruction Hour. Diagnosis of the heterophorias, James W. White. ¶ Reading of the Minutes. ¶ Case Reports—a] A further report on a case of lateral proboscis with cyclopean eye, Louise H. Meeker, Rudolph Aebli; b]Intrinsic variability of astigmatic errors, Joseph I. Pascal (by invitation). ¶ Papers of the Evening—a] Differential diagnosis of paresis of the obliques and superior or inferior rectus (*moving pictures*), W. Thornwall Davis, Washington, D. C. (by invitation). Discussion, James W. Smith; b] Effects on high altitude flying and deep sea diving on ocular function, Commander Leon D. Carson, M.C. USN (by invitation). ¶ Discussion, Conrad Berens.

FEBRUARY 29—*Section of Obstretics and Gynecology.* ¶ Executive Session, Reading of minutes. ¶ Case Report—Artificial insemination from donor. Clinical study of six successful cases and three failures. (*lantern slides*), Marie P. Warner (by invitation). ¶ Paper of the Evening. Treatment of uterine prolapse. (*Lantern slides*), H. W. Johnson (by invitation). ¶ General Discussion.

AFFILIATED SOCIETIES

FEBRUARY 16—*New York Section Society for Experimental Biology and Medicine in affiliation with The New York Academy of Medicine.* ¶ Papers of the Evening—a] Phosphorus metabolism in gravity-shocked rabbits, W. L. Nastuk (by invitation), (introduced by W. H. Cole); b] Two fractions of substances

in shed blood which contract smooth muscle, M. B. Zuker (by invitation), J. J. McBride (by invitation), C. Tsai (by invitation), (introduced by M. I. Gregersen); c] The determination of biological values of proteins, J. B. Allison (by invitation), J. A. Anderson (by invitation), R. D. Seeley (by invitation), (introduced by W. H. Cole); d] Remarks on the structure and properties of the thromboplastic protein, E. Chargaff, A. Benedich (by invitation), S. S. Cohen (by invitation), D. H. Moore (by invitation); e] The discrete extensor plantar response, a sign of extrapyramidal damage, F. A. Mettler; f] Arrest of endocarditis due to Streptococcus viridans, W. J. MacNeal, A. Blevins (by invitation), A. E. Slavkin (by invitation), C. A. Poindexter (by invitation); g] Combined penicillin and heparin treatment of subacute bacterial endocarditis; experimental and clinical study, L. Loewe (by invitation), R. Rosenblatt (by invitation), H. Greene (by invitation), M. Russell (by invitation), (introduced by W. J. MacNeal).

FEBRUARY 21—*The New York Roentgen Society in affiliation with The New York Academy of Medicine.* ¶ Papers of the Evening—a] Cartilaginous injuries of the knee joint as incurred in the Navy, Lt. Comdr. Marvin A. Stevens, M.C., USNR (by invitation). Discussion, Philip D. Wilson (by invitation); b] Some notes on the roentgen examination of the injured knee, Lt. Comdr. Jacob Gershon-Cohen, M.C., USNR (by invitation). Discussion, Raymond W. Lewis. ¶ General Discussion. ¶ Executive Session.

FEBRUARY 24—*The New York Pathological Society in affiliation with The New York Academy of Medicine.* ¶ Presentation of Cases. Histology of the lymphoid tissues in measles, Vera Dolgopol. ¶ Papers of the Evening—a] Experimental argyrosis, Charles T. Olcott; b] A comparative survey of diagnostic serologic findings in relation to syphilis, Howard Fox (by invitation), John F. Mahoney (by invitation). ¶ Executive Session.